Caring the Journey of Togetherness

Focus on : Respiratory Failure

20th

International Meeting on Respiratory Care Indonesia (Respina) 2018

Proceeding E-book

The 20ᵗʰ International Meeting on Respiratory Care Indonesia (Respina) 2018

Theme:
"Caring the Journey Togetherness"
Focus on: Respiratory Failure

Shangri-La Hotel Jakarta
July 20ᵗʰ -21ˢᵗ, 2018

The Society of Respiratory Care Indonesia (RESPINA)

Organizing Committee

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Editor:
Pompini Agustina, MD
Anitta FS Paulus, MD

Reviewer:
Menaldi Rasmin, MD
Ida Bernida, MD

Contents

Welcome Message

Dear Colleagues,

Wecome to Jakarta

On behalf of 20th Respina 2018 Organizing Committee, we extend a warm welcome to all participants to attend The International Meeting of Respiratory Care Indonesia which will be held on 17th - 21st July 2018 in Shangri-La hotel, Jakarta. Respina has been organized since 1998 as one of the largest Respiratory Care event in Southeast Asia.

Featuring the theme **"Caring the Journey of Togetherness, Focus on: Respiratory Failure".**

Respina will bring the to-date information and explore the latest development of medical science to overcome the global problems in respiratory care and as a media of collaboration for all respiratory care practitioners. Respina 2018 consists of three days of workshop and two days of scientific symposia.

There will be ten workshops, in which we collaborate with National Agency of Food and Drugs Control (Badan Pengawas Obat dan Makanan/BPOM) and National Institute of Health, Research, and Development (Badan Penelitian dan Pengembangan Kesehatan/Balitbangkes).

The scientific symposia will gather a number of prominent experts presenting plenary lectures as well as many more specific sessions. We do hope to create the attractive and knowledgeable conference. RespiQuizz will provide the chance to see the capabilities and competitiveness between students from various medical faculties in Indonesia. Last but not least, the novel studies and advancements in respiratory care will be presented by various specialists in poster session.

In conclusion, the 20th Respina will offer great opportunities for the participants to discuss recent topics regarding respiratory care in their respective expertise's and share their experiences in daily practice.

We are looking forward to see you in Jakarta to enjoy the excitement of this scientific meeting.

Warm Regards,

Santi Rahayu Dewayanti, M.D.
Chairperson of the Organizing Committee

About Respina 2018

Respiratory Care Indonesia (Respina) is an annual international meeting in Indonesia on respiratory care. Respina is a result of collaboration of five pillars, which are Department of Pulmonology and Respiratory Medicine Faculty of Medicine University of Indonesia, American College of Chest Physician-Indonesia Chapter, Asian Pacific Society of Respirology, Indonesia Society of Bronchoscopy and Indonesian Society of Respirology, in answering the global problem of respiratory care. The mission of the meeting is to bring the up-to-date and latest information of respiratory care and as media of collaboration to each respiratory care practitioners in cooperative spirit.

Starting on 2006, Respina is proudly joined by societies that shared the same interest particularly in respiratory care, and they are as follows:
- Indonesian Society of Respirology
- Indonesian Association of Thoracic and Cardiovascular Surgeons
- Indonesian Radiological Society
- Indonesian Neurological Association
- Indonesian Heart Association
- The Indonesian Society of Anesthesiology and Intensive Therapy
- The Indonesian of Physical Medicine and Rehabilitation Association
- Indonesian Pediatric Society
- The Indonesian Otorhinolaryngological Head and Neck Surgery Society

Four other professional organizations joined Respina in 2011, they are:
- Indonesian Association of Clinical Pathologists
- The Indonesian Physician of community medicine and Public Health Association
- Indonesian Sports Medicine Association
- Indonesian Society for Clinical Microbiology

Respina 2018 is the 20th meeting we have been conducting and during the years, Respina has become one of the major respiratory events in Indonesia and gained greater and still growing interest from physicians across the regions, particularly from our colleagues in Southeast Asia.

Society by:

Organizing Committee

PILLAR
- Department of Pulmonology and Respiratory Medicine Faculty of Medicine University of Indonesia
- American College of Chest Physician (ACCP) - Indonesian Chapter
- Asian Pacific Society of Respirology (APSR) Representative for Indonesia
- The Indonesia Society of Bronchoscopy (PERBRONKI) Indonesia
- Indonesian Society of Respirology (PDPI)

HONORARY CHAIR
- Prof. Hadiarto Mangunnegoro, MD, FCCP
- Venugopal S. Reddy, MD, FCCP

BOARD COMMISION
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- Dicky Soehardiman, MD
- Amira Anwar, MD
- R. Fajar Prosojo Utomo, MD

INVITED SPEAKERS
- Amanda Piper (AUS)
- Caleste Mae Campomanes (PHI)
- Cesare Gregoretti (ITA)
- Chitra Mehta (IND)
- Franco Laghi (USA)
- Gary Lee (AUS)
- Jennifer Ann Mendoza-Wi (PHI)
- Martin J. Tobin (USA)
- Nicolino Ambrosino (ITA)
- Philip Eng (SIN)
- Ronald F. Grossman (CAN)
- Sangeeta Mehta (CAN)
- Venugopal S. Reddy (USA)

Faculty Members

Cesare Gregoretti,
Director of General Intensive Care Unit and Anesthesiology Service Orthopedic and Trauma Center of Turin, Italy.
Independent referee of international journals such as Intensive Care Medicine, European Respiratory Journal, Respiratory Medicine.
Professor of Intensive Care and Anesthesiology at the postgraduate school, University of Turin and Novara Italy.
Speaker and chairman at main national and international conventions in the field of mechanical ventilation and an Invited Professor at Tuft University in Boston and Temple University in Philadelphia.

Jennifer Ann Mendoza-Wi
Full Professor Lyceum Northwestern FQ Duque College of Medicine, Dagupan City.
International Governor, American College of Chest Physicians, Philippine Chapter.

Martin Tobin
Professor of Medicine, Pulmonary and Critical Care Medicine.
Division Director, Pulmonary & Critical Care Medicine Special Interests: Acute Respiratory Failure.
Neuromuscular Control of Breathing Mechanical Ventilation.

Neil Ross Macintyre, JR
Professor of Medicine
Duke University Medical Center
Chief of Clinical Services
Division of Pulmonary and Critical Care Medicine
Medical Director of Respiratory Care Services,
Pulmonary Function Laboratory, and Pulmonary Rehabilitation Program
Duke University Medical Center
Durham, NC

Nicolino Ambrosino
Appointed Professor of Universities of Pisa, Pavia, Firenze, Trieste, Milano
Professor Head, Pulmonary Department, Cardio-Thoracic Department, University Hospital, Pisa.
Head, Pulmonary Unit, Respiratory Intensive Care. Cardio-Thoracic Department, University Hospital, Pisa.
Head, Pulmonary Rehabilitation and Weaning Center, Auxilium Vitae, Volterra
Scientific Director of Auxilium Vitae, Volterra
Former Head : Pulmonary Division and Intermediate Intensive Care. Medical Center of Gussago, S. Maugeri Foundation

Paolo Navalesi
Ospedale Maggiore della Carità in Novara (Italy).
Head of the Intensive Care Unit of the Department of Anesthesia and Intensive Care.
Teaches at the School of Anesthesiology and Intensive Care of The University of the Oriental Piedmont.

Richard Wayne Light
Practices Internal Medicine, Pulmonary Disease near Nashville, TN.
Professor of Medicine, Vanderbilt University, Nashville.
Professor Emeritus of Medicine, University of California at Irvine

Venugopal S Reddy
Associate Professor of Anesthesia and Critical Care Medicine.
Divisional Director Critical Care Medicine
Director of Surgical Anesthesia Intensive Care Unit.
Director of Mortality and Morbidity meeting Penn State College of Medicine and Hershey Medical Center, Hershey, USA.

Scientific Program

DAY 1 FRIDAY, 20th July 2018			
REGISTRATION			
MORNING SYMPOSIUM 1 Chance to Prevent Respiratory Failure	**MORNING SYMPOSIUM 2** Cardiovascular	**MORNING SYMPOSIUM 3** Fluid and Electrolyte	
PLENARY SESSION 1 Essence of Respiratory Failure			
OPENING CEREMONY			
MASTER CLASS ON RESPIRATORY FAILURE Caring Togetherness of Respiratory Failure (EU & ASIA)	**MASTER CLASS ON RESPIRATORY FAILURE** Caring Togetherness of Respiratory Failure (ASIA & AUS)	**MASTER CLASS ON RESPIRATORY FAILURE** Caring Togetherness of Respiratory Failure (USA & ASIA)	
LUNCH & FRIDAY PRAYING			
MEET THE EXPERT 1 Respiratory Failure in Emergency	**MEET THE EXPERT 2** Respiratory Failure in the Ward	**MEET THE EXPERT 3** Respiratory Failure in Intensive Care Unit	
SATELLITE SYMPOSIUM 1 Respiratory Failure : Daily Practice	**SATELLITE SYMPOSIUM 2** Neuromuscular	**SATELLITE SYMPOSIUM 3** Small Airway	
SATELLITE SYMPOSIUM 4 Chronic Respiratory Failure in Pulmonary Fibrosis : Understanding Goals of the Treatment	**SATELLITE SYMPOSIUM 5** Making New Links : Mechanism of Organ Failure in Sepsis and ARDS	**SATELLITE SYMPOSIUM 6** NIV in Respiratory Failure	**FREE PAPER & POSTER SESSION**
STUDIUM GENERALE Medicine: Art or Science			

Scientific Program

DAY 2 SATURDAY, 21st July 2018

REGISTRATION		
MORNING SYMPOSIUM 4 Respiratory Failure in Pediatrics	**MORNING SYMPOSIUM 5** Interventional Procedure in ICU	**MORNING SYMPOSIUM 6** Respiratory Failure in Special Conditions

PLENARY SESSION 2 Insight in Critical Care : Never Ending Challenge

RespiQuizz

LESSON'S LEARNED Myelitis Presenting as GBS with Respiratory Failure

SATELLITE SYMPOSIUM 7 Mucous Management to Avoid Repiratory Failure	**SATELLITE SYMPOSIUM 8** Prevention Respiratory Failure in Chronic Obstructive Pulmonary Disease	**SATELLITE SYMPOSIUM 9** Cilinical Review of Asthma

LUNCH & PRAYING

LUNCH SYMPOSIUM 2 Obstructive Pulmonary Disease Highlight

SATELLITE SYMPOSIUM 10 Respiratory Failure: The Role of Infection	**SATELLITE SYMPOSIUM 11** Inflammation Storm in Respiratory Failure	**SATELLITE SYMPOSIUM 12** Respiratory Failure: Why it is Prolonged?
SATELLITE SYMPOSIUM 13 Non-Invasive Ventilation in Respiratory Failure	**SATELLITE SYMPOSIUM 14** Mechanical Ventilation in Respiratory Failure	**SATELLITE SYMPOSIUM 15** Rehabilitation Program in ICU

SUMMARY Practice Respiratory Failure Pathway for General Practitioners : Conclusion Remarks

CLOSING CEREMONY

Scientific Schedule

REGISTRATION
07.00 - 07.30

MORNING SYMPOSIUM 1
Chance to Prevent Respiratory Failure

07.30 - 07.50	Global Burden of Respiratory Diseases in Indonesia
	Siswanto Agus Wilopo (INA)
07.50 - 08.10	General Exercise Training
	Rika Haryono (INA)
08.10 - 08.15	Discussion

MORNING SYMPOSIUM 2
Cardiovascular

07.30 - 07.50	Cardiopulmonary Edema in Respiratory Failure
	Daniel PL Tobing (INA)
07.50 - 08.10	Pulmonary Hypertension in Respiratory Failure
	Andika Chandra Putra (INA)
08.10 - 08.15	Discussion

MORNING SYMPOSIUM 3
Fluid and Electrolyte

07.30 - 07.50	Body Fluid in Respiratory Failure
	Bambang Pudjo Semedi (INA)
07.50 - 08.10	Electrolyte and Respiratory Failure
	Navy Lolong (INA)
08.10 - 08.15	Discussion

PLENARY SESSION 1
Essence of Respiratory Failure

08.15 - 08.35	Respiratory Failure : How to Win the Battle (An Overview)
	Venugopal S. Reddy (USA)
08.35 - 09.05	How to use ICU Monitoring Data to Make Wise Clinical Decisions
	Martin J. Tobin (USA)
08.35 - 09.05	Ethical Aspect in Respiratory Failure
	Ike Sri Redjeki (INA)

OPENING CEREMONY
09.25 - 10.35

MASTER CLASS ON RESPIRATORY FAILURE
Caring Togetherness of Respiratory Failure (EU & ASIA)

10.35 - 11.00	World Perspective of Respiratory Failure: Europe
	Nicolino Ambrosino (ITA)
11.00 - 11.25	World Perspective of Respiratory Failure: Asia
	Chitra Mehta (IND)
11.25 - 11.30	Discussion

MASTER CLASS ON RESPIRATORY FAILURE
Caring Togetherness of Respiratory Failure (ASIA & AUS)

10.35 - 11.00	World Perspective of Respiratory Failure: Asia
	Menaldi Rasmin (INA)
11.00 - 11.25	World Perspective of Respiratory Failure: Australia
	Amanda Piper (AUS)
11.25 - 11.30	Discussion

MASTER CLASS ON RESPIRATORY FAILURE
Caring Togetherness of Respiratory Failure (USA & ASIA)

10.35 - 11.00	World Perspective of Respiratory Failure: USA
	Franco Laghi (USA)
11.00 - 11.25	World Perspective of Respiratory Failure: Asia
	Phillip Eng (SIN)
11.25 - 11.30	Discussion

LUNCH & FRIDAY PRAYING
11.30 - 13.00

MEET THE EXPERT 1
Respiratory Failure in Emergency

13.00 - 13.25	Respiratory Failure : Pharmacotherapy
	Oloan Tampubolon (INA)
13.25 - 13.30	STRETCHING
13.30 - 13.55	The Algorithm
	Franco Laghi (USA)
13.55 - 14.05	Discussion

MEET THE EXPERT 2
Respiratory Failure in the Ward

13.00 - 13.25	Beware of Distress
	Menaldi Rasmin (INA)
13.25 - 13.30	STRETCHING
13.30 - 13.55	How to Avoid Failure
	Ike Sri Redjeki (INA)
13.55 - 14.05	Discussion

MEET THE EXPERT 3
Respiratory Failure in Intensive Care Unit

13.00 - 13.25	Respiratory Failure : Respiratory Monitoring
	Navy Lolong (INA)
13.25 - 13.30	STRETCHING
13.30 - 13.55	How to Wean a Patient as Early as Possible
	Venugopal S. Reddy (USA)
13.55 - 14.05	Discussion

Scientific Schedule

SATELLITE SYMPOSIUM 1
Respiratory Failure: Daily Practice

14.05 - 14.25	Practical Aspects of the Type of Respiratory Failure *Dwi Pantja Wibowo (INA)*
14.25 - 14.45	Viruses and Respiratory Failure *Philip Eng (SIN)*
14.45 - 15.00	Discussion

SATELLITE SYMPOSIUM 2
Neuromuscular

14.05 - 14.25	The Role of Neuromuscular and Respiratory Failure *Amanda Piper (AUS)*
14.25 - 14.45	Maintaining Neuromuscular in Mechanical Ventilation Patient *Manfaluthy Hakim (INA)*
14.45 - 15.00	Discussion

SATELLITE SYMPOSIUM 3
Small Airway

14.05 - 14.20	Pulmonary Embolism : "The Role of Great Saphenous Vein Dilatation" *Ismoyo Sunu (INA)*
14.20 - 14.35	Small Airway in Obstructive Pulmonary Disease *Hadiarto Mangunnegoro (INA)*
14.35 - 14.50	Caring Near Fatal Asthma *Retno Wihastuti (INA)*
14.50 - 15.00	Discussion

SATELLITE SYMPOSIUM 4
Chronic Respiratory Failure in Pulmonary Fibrosis :
Understanding Goals of the Treatment

15.00 - 15.25	Imaging of Pulmonary Fibrosis: Diagnostic Approach *Aziza G. Icksan (INA)*
15.25 - 15.50	Management of Pulmonary Fibrosis with Chronic Respiratory Failure : Pharmacotherapy and NIV *Faisal Yunus (INA)*
15.50 - 16.00	Discussion

SATELLITE SYMPOSIUM 5
Making New Links : Mechanism of Organ Failure in Sepsis and ARDS

15.00 - 15.25	Cardiovascular Complication of Sepsis Due to LRTI *Ronald F. Grossman (CAN)*
15.25 - 15.50	Microbiom : Risk Factor on Respiratory Failure *Kuntaman (INA)*
15.50 - 16.00	Discussion

SATELLITE SYMPOSIUM 6
NIV in Respiratory Failure

15.00 - 15.25	Consideration Usage in Acute and Chronic Respiratory Failure *Prasenohadi (INA)*
15.25 - 15.50	Complication of NIV *Cesare Gregoretti (ITA)*
15.50 - 16.00	Discussion

FREE PAPER
15.00 - 16.00

POSTER SESSION
15.00 - 16.00

STUDIUM GENERALE

16.00-17.00	Medicine: Art or Science *Martin J. Tobin (USA)*

Scientific Schedule

DAY 2 SATURDAY, 21st JULY 2018

REGISTRATION
07.00 - 07.30

MORNING SYMPOSIUM 4
Respiratory Failure in Pediatrics

07.30 - 07.50	Initial Assesment and Ventilatory Strategy for Acute Respiratory Failure in Infant *Rismala Dewi (INA)*
07.50 - 08.10	NIV in OSA : Focus to Failure *Bambang Supriyatno (INA)*
08.10 - 08.30	Pitfalls in Neonates Respiratory Failure *Agnes Yunie Purwita Sari (INA)*
08.30 - 08.35	Discussion

MORNING SYMPOSIUM 5
Interventional Procedure in ICU

07.30 - 07.50	Timing of Central Venous Cannulation in Septic Shock and Respiratory Arrest *Ronggo Prakoso (INA)*
07.50 - 08.10	Airway Management in Respiratory Failure *Wahju Aniwidyaningsih (INA)*
08.10 - 08.30	Tracheostomy in Prolonged Ventilator *Syahrial M. Hutauruk (INA)*
08.30 - 08.35	Discussion

MORNING SYMPOSIUM 6
Respiratory Failure in Special Conditions

07.30 - 07.50	Sepsis and Respiratory Failure *Ronald F. Grossman (CAN)*
07.50 - 08.10	First Line Antibiotic in Sepsis *Sutji A. Mariono (INA)*
08.10 - 08.30	Mediastinal Tumor and Respiratoy Failure *Paul Tahalele (INA)*
08.30 - 08.35	Discussion

PLENARY SESSION 2
Insight in Critical Care : Never Ending Challenge

08.35 - 09.05	The Outbreak: Diphtery *Rita Rogayah (INA)*
09.05 - 09.35	What Do ICU Patients Recall of Their Experience in ICU? *Sangeeta Mehta (CAN)*

RESPIQUIZZ
09.35-10.35

LESSON'S LEARNED
Myelitis Presenting as GBS with Respiratory Failure

10.35 - 10.40	Anchor: *Anitta F.S. Paulus (INA)*
10.40 - 10.45	GBS and Myelitis: How They Influence Respiratory Neuromuscular *Manfaluthy Hakim (INA)*

10.45 - 10.50	The Impact of Neuromuscular Disorders in Respiratory Failure *Faisal Yunus (INA)*
10.50 - 10.55	ICU Approach on Respiratory Failure Due to Neuromuscular Disorders *Oloan Tampubolon (INA)*
10.55 - 11.15	Discussion
11.15 - 11.25	Over-All View Respiratory Failure on Neuromuscular Disorders *Franco Laghi (USA)*
11.25 - 11.30	Question and Answer *Franco Laghi (USA)*
11.30 - 11.35	Conclusion

SATELLITE SYMPOSIUM 7
Mucous Management to Avoid Repiratory Failure

11.35 - 11.55	The Kinetic Role of Ciliary Clearance *Sita L. Andarini (INA)*
11.55 - 12.15	Management of Recurrent Cough in Children *Nastiti Kaswandani (INA)*
12.15 - 12.35	The Latest Study Regarding the Role of Mucoactive Tetradynamic on COPD Exacerbation *Susanthy Djajalaksana (INA)*
12.35 - 12.45	Discussion

SATELLITE SYMPOSIUM 8
Prevention Respiratory Failure in Chronic Obstructive Pulmonary Disease

11.35 - 11.55	Early Recognation of Acute and Chronic Respiratory Failure *Prasenohadi (INA)*
11.55 - 12.15	Prevention Respiratory Failure: Maximizing the Treatment for COPD Exacerbation *Wiwien Heru Wiyono (INA)*
12.15 - 12.35	Cardiovascular Approach in Chronic Respiratory Failure *Pradana Tedjasukmana (INA)*
12.35 - 12.45	Discussion

SATELLITE SYMPOSIUM 9
Clinical Review of Asthma

11.35 - 11.55	Respiratory Failure in Uncontrolled Asthmatic Patient *Cesare Gregoretti (ITA)*
11.55 - 12.15	The Strategy to Control Asthma *Pradjnaparamita (INA)*
12.15 - 12.35	Chronic Pulmonary Problem: Uncontrolled Asthma, In Rehabilitation Perspective *Nury Nusdwinuringtyas (INA)*

Scientific Schedule

12.35 - 12.45   Discussion

LUNCH
12.45 - 13.30

LUNCH SYMPOSIUM 2
Obstructive Pulmonary Disease Highlight
13.30 - 14.00   Current Care to Improve the Outcome of
                 COPD
                 Celeste Mae Campomanes (PHI)
14.00 - 14.05   STRETCHING
14.05 - 14.35   Asthma Control: Pharmacotherapy
                 Budhi Antariksa (INA)

SATELLITE SYMPOSIUM 10
Respiratory Failure : The Role of Infection
14.35-15.00   From Infection to Respiratory Failure
               Ronald F. Grossman (CAN)
15.00-15.25   Fungal Infection in Respiratory Failure
               Retno Wahyuningsih (INA)
15.25-15.35   Discussion

SATELLITE SYMPOSIUM 11
Inflammation Storm in Respiratory Failure
14.35-15.00   Inflammation Biomarker in Respiratory
               Failure
               Tony Loho (INA)
15.00-15.25   Strategies to Overcome Inflammation in
               Acute and Chronic Respiratory Failure
               Dianiati K. Sutoyo (INA)
15.25-15.35   Discussion

SATELLITE SYMPOSIUM 12
Respiratory Failure : Why It Is Prolonged?
14.35-15.00   Long-Term Prognosis of Respiratory Failure
               Patients
               Prasenohadi (INA)
15.00-15.25   Respiratory Failure : Facing the Unsolved
               Result
               Navy Lolong (INA)
15.25-15.35   Discussion

SATELLITE SYMPOSIUM 13
Non-Invasive Ventilation in Respiratory Failure
15.35 - 16.00   Various Condition that Can be Treated With
                 NIV
                 Dicky Soehardiman (INA)
16.00 - 16.25   NIV Setting and Monitoring
                 Nicolino Ambrosino (ITA)
16.25 - 16.35   Discussion

SATELLITE SYMPOSIUM 14
Mechanical Ventilation in Respiratory Failure
15.35 - 16.00   Difficult to Wean in Infant to Children
                 Yogi Prawira (INA)
16.00 - 16.25   Home Mechanical Ventilation
                 Oloan Tampubolon (INA)
16.25 - 16.35   Discussion

SATELLITE SYMPOSIUM 15
Rehabilitation Program in ICU
15.35 - 16.00   Early Mobilization and Rehabilitation
                 Program in Intubated Patients
                 Anitta F.S. Paulus (INA)
16.00 - 16.25   Family Presence in the ICU
                 Sangeeta Mehta (CAN)
16.25 - 16.35   Discussion

SUMMARY
16.35 - 17.05   Practice Respiratory Failure Pathway for
                 GP : Conclusion Remarks
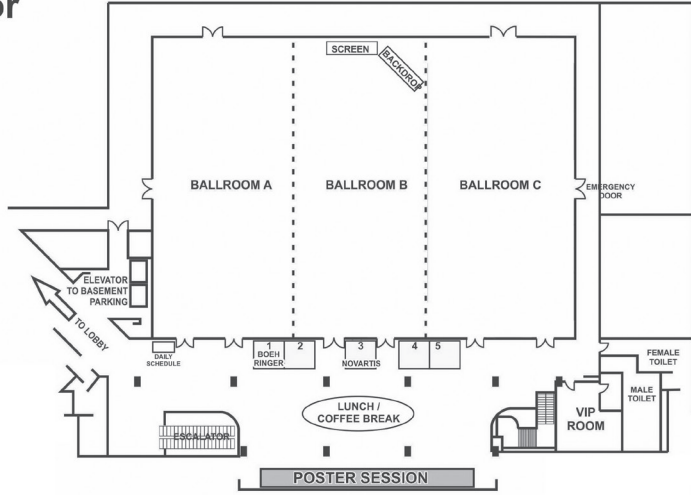   *Menaldi Rasmin (INA)*

CLOSING CEREMONY
17.05 - 17.25

Exhibition Floor Plan

THE 20 INTERNATIONAL MEETING of
RESPIRATORY CARE INDONESIA (RESPINA)
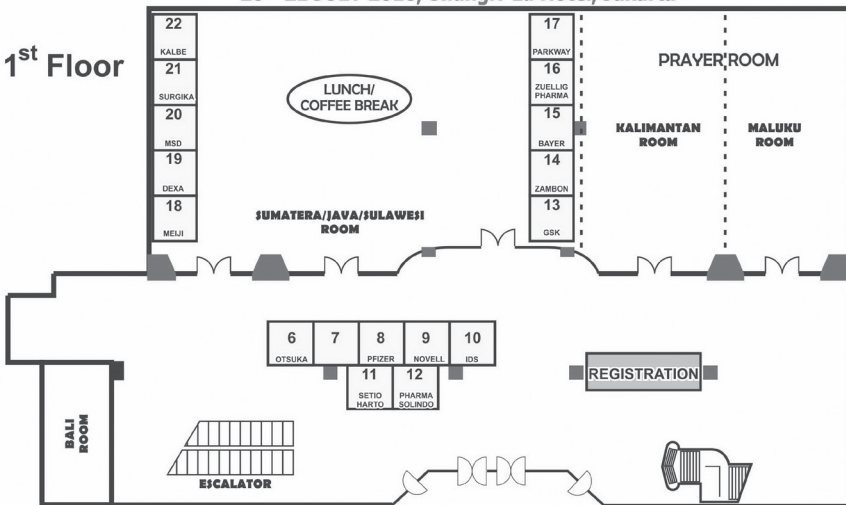20 - 21 JULY 2018, Shangri-La Hotel, Jakarta

2nd Floor

SCREEN BACKDROP

BALLROOM A   BALLROOM B   BALLROOM C   EMERGENCY DOOR

ELEVATOR TO BASEMENT PARKING
TO LOBBY
DAILY SCHEDULE
1 BOEH RINGER 2 3 NOVARTIS 4 5
FEMALE TOILET
MALE TOILET
ESCALATOR
LUNCH / COFFEE BREAK
VIP ROOM
POSTER SESSION

Ukuran Stand: 3m x 3m

THE 20th INTERNATIONAL MEETING of
RESPIRATORY CARE INDONESIA (RESPINA)
20 - 21 JULY 2018, Shangri-La Hotel, Jakarta

1st Floor

22 KALBE
21 SURGIKA
20 MSD
19 DEXA
18 MEIJI

LUNCH/ COFFEE BREAK

17 PARKWAY
16 ZUELLIG PHARMA
15 BAYER
14 ZAMBON
13 GSK

PRAYER ROOM

KALIMANTAN ROOM   MALUKU ROOM

SUMATERA/JAVA/SULAWESI ROOM

6 OTSUKA 7 8 PFIZER 9 NOVELL 10 IDS
11 SETIO HARTO 12 PHARMA SOLINDO

REGISTRATION

BALI ROOM

ESCALATOR

Ukuran Stand: [ ] Retail Booth 3m x 3m

Exhibitor List

NO. BOOTH	COMPANY
1.	Boehringer Ingelheim
3.	Novartis Indonesia
6.	Otsuka Indonesia
8.	Pfizer Indonesia
9.	Novell Indonesia
10.	IDS Medical System
11.	Setio Harto
12.	Pharmasolindo
13.	Glaxo Smith Kline
14.	Zambon
15.	Bayer Indonesia
16.	Anugrah Pharmindo Lestari (Zuelligpharma)
17.	Parkway Hospitals Singapore
18.	Meiji Indonesia
19.	Dexa Medica
20.	Surgika Alkesindo
21.	Kalbe Farma

Acknowledgement

1. **Novartis Indonesia**

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3. **Dexa Medica**

4. **Astra Zeneca Indonesia**

5. **Zambon Indonesia**

6. **Setio Harto**

7. **Boehringer Ingelheim**

8. **Pfizer Indonesia**

9. **Pharmasolindo**

10. **IDS Medical System**

11. **Novell Indonesia**

12. **Otsuka Indonesia**

13. **Darya Varia**

14. **Meiji Indonesia**

15. **Surgika Alkesindo**

16. **Bayer Indonesia**

17. **Kalbe Farma**

18. **Prodia Laboratories**

19. **Parkway Hospitals Singapore**

20. **Anugrah Pharmindo Lestari (Zuelligpharma)**

Abstract Contents

Abstract Contents

Abstract Contents

FRIDAY, 20th JULY 2018

GLOBAL BURDEN OF RESPIRATORY DISEASES IN INDONESIA

Siswanto Agus Wilopo
[1]Professor of Department of Biostatistics, Epidemiology and Population Health
[2]Center for Reproductive Health
Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada
[3]Adjunct Full Professor, University College Dublin, Ireland

ABSTRACT

Background: Information on the burden of respiratory diseasesis essential for health promotion and prevention of the respiratory diseases but is lacking in Indonesia.

Objectives: To examine the importance of burden of respiratory diseases in Indonesia compared to global and other ASEAN countries figures using data from the Global Burden of Disease (GBD) Study in 2015.

Methods: We considered tuberculosis, lower and upper respiratory infections, Chronic Obstructive Respiratory Diseases (COPD), asthma and pneumoconiosis included in GBD Study 2015. We performed reviews of these epidemiological data and data were modelled using a Bayesian meta-regression tool to produce prevalence estimates by age, sex, and year for Global, Indonesia, Malaysia and Thailand. As a measure of non-fatal burden, prevalence for each respiratory disease was then combined with a disorder-specific disability weight to give years lived with disability (YLDs). Fatal burden was measured as years of life lost (YLLs) due to premature mortality and it was calculated by combining the number of deaths due to a disorder with the life expectancy remaining at the time of death. A measure of total burden disability-adjusted life years (DALYs) was calculated by summing YLDs and YLLs.

Results: Globally in 2016, respiratory diseases contributed 6.59 million deaths annually. Diseases were also significantly causes of fatal burden in Indonesia and its contributed more than 211 thousand deaths annually. These numbers for Malaysia and Thailand are 22 and 64.6 thousandrespectively. Tuberculosis is the most common cause of death and it is followed by COPD, lower respiratory infection and asthma in Indonesia. At Global level COPD is the common cause of death while lower respiratory infectionisthe most common cause of death in Malaysia and Thailand. Among more than 229.126 million DALYs at Global level, Indonesia contributes more than 8.057 million DALYs or about 3.5 % of global DALYs. Tuberculosis has higher percentage of total DALYS (4.2%) in Indonesia and it is followed lower respiratory infection (2.4%), COPD (2.2%) and asthma (1.9%). Thailand and Malaysia are dominated by lower respiratory infections. We examinedchanges of the disease burden in the past decade also prevalenceamong male and female as well as by age groups.

Conclusion: GBD Study 2015 found that were significant contributors of respiratory disease to disease burden in Indonesia during 2016. Tuberculosis is the most significant burden compared to other diseases and it is followed by lower respiratory infection. At the global level, COPD is the most significant problems while the lower respiratory infection is the most common problem in Malaysia and Thailand.

Key Words: Epidemiology, burden of diseases, respiratory, Indonesia-Malaysia-Thailand

IMPORTANT DATA OF RESPIRATORY FAILURE

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ABSTRACT

Introduction

Cardiorespiratory fitness is one of physical fitness component which usually obtained by measure VO2max. Aerobic training improves both cardio and respiratory function at once and therefore improves VO2 as well. VO2max and pulmonary function influence each other. The purpose of this study is to examine the relationship between VO2max and pulmonary function.

Material and methods

A cross sectional study involved thirty male adolescent aged 18 to 19 years old. VO2max was examined by using Queen's College Step test with equation formula. Pulmonary function such as VC, FVC, and FEV1 were measured by spirometry. Pearson correlation test was apllied to examine the relationship between VO2max and VC, FVC and FEV1. Informed consent was obtained from each subject with signing.

Result

Most subjects had low VO2max (25% in average and 75% in below average categories according to age and gender). Mean of vital capacity (VC) was $4.75 + 1.5$ L/min (97 % from predicted value), Force Vital Capacity (FVC) was $3.3 + 1.1$ L/min (72% from predicted value)) and FEV1 was $3.1 + 1.0$ L/min (73% from predicted value). The result of this study clearly showed a positive correlation between VO2max and VC, FVC and FEV1 ($p = 0.04$, $p = 0.01$ and $p = 0.01$) respectively.

In conclusion: VO2max was correlated with pulmonary function in male adolescent.

Keywords: general exercise training, cardiorespiratory fitness, pulmonary function, male adolescent

BODY FLUID IN RESPIRATORY FAILURE

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ABSTRACT

Maintaining body fluids balance is essential in treating critically ill patients. Many scientific evidences support that intravascular volume deficit as well as excess fluid will increase morbidity and mortality.

Management of early resuscitation in hypotensive critically ill patients is almost always associated with aggressive fluid resuscitation. Consequently, fluid overload from positive fluid balance is often seen after resuscitation, especially in patients with a fluid retention tendency such as congestive heart failure and acute renal failure[1]. Fluid overload can lead to hypertension, arrhythmia, congestive heart failure2, difficulty in weaning from mechanical ventilation, lengthening hospitalization duration and proven to aggravate the condition of the patient with critical illness[3-5].

In the case of sepsis, positive fluid balance at baseline can be used as a predictor of mortality within the next 28 days[6,7]. Fluid overload has shown to be associated with increased morbidity and mortality in cancer[8], intracranial hemorrhage[9], and lung damage[10,11]patients undergoing ICU treatment. Fluid overload triggers interstitial edema and fluid extravasation into the third cavity, which further adversely affects the organ system. Disorders of the organ system may be caused by damage to the myocardium, central nervous system, hepatic disturbance, and digestive system dysfunction resulting in nutrients malabsorption syndrome[12]. Liberal fluid administration strategies result in increased morbidity and mortality rates in postoperative, traumatized, and ARDS patients[13-15]. Meanwhile, restrictive fluid strategies are reported to provide better results, especially in patients with congestive heart failure and acute renal failure[2].

Oxygenation disorders due to accumulation of fluid in the lungs were often found in ICU. This condition is generally caused by heart failure due to fluid overload and a severe inflammatory process that results in ARDS. In studies on subjects of children with ARDS, it has been shown that fluid overload is associated with increased mortality and prolonged use of mechanical ventilation as a result of worsening oxygenation ability[12,16].

Under normal circumstances, fluid and protein accumulation in the interstitial compartment is prevented through the process of recirculating fluids from the interstitial to the intravascular compartment via the lymphatic system. Theoretically, the entire volume of plasma fluid will surely pass through the vascular membrane to the extravascular space and back into the circulation. The process will occur at least once a day. However, in pathological conditions such as trauma or sepsis, the process can occur repeatedly in a day[17].

The process of accumulation of plasma fluid in the interstitial that causes hypovolemia and tissue edema is not only caused by disruption of microvascular permeability to fluids and proteins only. The capacity of the lymphatic system as well as other factors, such as capillary hydrostatic pressure, the type of plasma volume expander used and the intravenous fluid selection strategy have greatly affected this process[17].

Sepsis patients often experience respiratory failure, either caused by excessive fatigue or due to the disease process itself (eg pneumonia and / or ARDS). Pneumonia patients are not infrequently experiencing septic shock requiring fluid resuscitation. Management of improper fluid will only worsen the situation.

In order to avoid early post-resuscitation complications, negative fluid balance should be considered if hemodynamic stability can be maintained with minimal vasopressor administration and mechanical ventilation support can be reduced. Management of restrictive fluid after resuscitation aims to reduce the impact of fluid overload that is difficult to avoid. However, it is important to maintain the mean arterial pressure (MAP) within the range of autoregulation so that renal perfusion is met and production targets can be achieved[18]. The administration of albumin may be considered especially in septic patients to maintain intravascular oncotic pressure[19]. Diuretics are a pharmacological therapy modality often used in fluid overload. Renal replacement therapy (RRT) is the last modalities when various therapies have been unable to reduce fluid retention in critically ill patients[12].

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WORLD PRESPECTIVE OF RESPIRATORY FAILURE : EUROPE
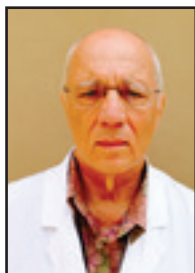
Nicolino Ambrosino
ITA

ABSTRACT

The increasing worldwide life expectancy results in high prevalence of patients suffering from chronic diseases and related "chronic critical illness". Up to 20 million people annually require Intensive Care Units (ICUs) admission and mechanical ventilation. The progresses in management of these patients has improved their short-term survival at the price of a growing population of patients with partial or complete dependence on mechanical ventilation. The prevalence of ventilator assisted individuals ranges from 6.6 (in Europe) to 23 per 100,000 resulting in difficult clinical and organizational problems for patients, caregivers and health services, as well as high human and financial resources consumption, despite poor long-term outcomes.

In 2010 the German Society of Pneumology recommended that the presence of symptoms linked to chronic respiratory failure, poor quality of life, and at least one of the following criteria could indicate the need for long-term ventilatory support in COPD patients:

- chronic daytime hypercapnia with $PaCO2 \geq 50$ mmHg

- nocturnal hypercapnia with $PaCO2 \geq 55$ mmHg

- stable daytime hypercapnia with PaCO2 ranging46–50 mmHg and a rise in transcutaneous $CO2 \geq 10$ mmHg during sleep

- stable daytime hypercapnia with PaCO2 46–50 mmHg and at least 2 acute acidotic exacerbations with hospital admission in the last 12 months need of prolonged ventilatory support following an acute exacerbation

WORLD PRESPECTIVE OF RESPIRATORY FAILURE : EUROPE

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ABSTRACT

Acute respiratory failure (ARF) is one of the common and serious complication among hospitalised patients. It may develop as a result of pneumonia, chronic obstructive pulmonary disease (COPD), acute respiratory distress syndrome (ARDS) and congestive heart failure. ARF is associated with high global morbidity and mortality. The majority of epidemiological studies on ARF are restricted to intensive care patients, especially those requiring mechanical ventilation. Despite the enormous socioeconomic and geographical impact on respiratory failure, there are limited studies from asia.

Asia is the most populated continent containing around 60% of the world's population. It mostly comprises of low and middle income countries. This area generally faces the challenge of overcrowding, poverty and limited healthcare resources.

ARDS has been found to be the leading cause of ARF in asia, similar to the western countries. The famous LUNG- SAFE study extrapolated that a typical 10- bed ICU in Asia would see 35 patients with ARDS per year as compared to 74 patients for a similar size unit in North America. The overall mortality of ARDS in this study was found to be 42.8%.The incidence of ARDS was found to be around 0.27 cases/ICU bed/ year in Asia.

Only a few studies on ARDS have been conducted from asia. Majority of these are from India. Average ARDS related mortality was found to be 40% from Taiwan, 52.5% from Japan. Mortality from India has been reported to be around 45% to 50%. Most of these figures are higher than those reported from western countries. These studies have found infectious etiology for ARDS to be more common.Infective causes of ARDS in the tropical zone are distinct compared to the temperate countries. Though bacterial pneumonias remain most common, tropical diseases like malaria, scrub typhus, dengue, tuberculosis and leptospirosis are encountered far more commonly. Clinical presentation of ARDS and patterns of care have been found to vary significantly across geo-economic groups of countries defined by gross national income per person.

Similar to western countries, streptococcus pneumoniae has been found to be the most common organism associated with pneumonia in asian countries. Infection with atypical organisms like mycoplasma, chlamydia and legionella are less common. Pneumonia secondary to mycobacterium tuberculosis, burkholderia pseudomallai and klebsiella pneumonia seem to be more of a concern.

Transmissible infection related respiratory failure are a major cause of morbidity and mortality in asia. Beyond tuberculosis, it is the recent epidemic of avian influenza, SARS, H1N1 influenza and MERS which have predominated the scene.

Other common cause of acute respiratory failure is acute exacerbation of COPD. Prevalence of COPD has been found to be around 8% in north asia, and about 4% in south east asian countries. The WHO has estimated that the number of COPD cases in asia may exceed the total number of COPD cases for the rest of the world by three fold.

Among the COPD patients, a noticeable proportion had visited the emergency department (7.6%) or been hospitalized (6.3%) in APBORD study.This may point to COPD patients being undertreated, and could be related to high cost of COPD medications.

Asia represents a mix of countries with all worldclass healthcare facilties, as well as those countries with large rural population with access to basic medical facility only. ARDS secondary to septic abortion, chorioamnionitis and amniotic fluid embolism is frequently seen among rural population.

There is a definite need to study the profile of respiratory failure in asia. Future directions of research should focus on identification of the mechanisms primary prevention and early treatment, as well as on targeted pharmacological therapies for this devastating condition.

WORLD PERSPECTIVE OF RESPIRATORY FAILURE: AUSTRALIA HOME VENTILATION AND CHRONIC HYPOVENTILATION SYNDROMES

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ABSTRACT

Chronic hypoventilation is a characteristic of a number of disorders, arising when there is an imbalance between neuromuscular capacity and respiratory load, with or without an additional impairment in respiratory drive. The introduction of long term home mechanical ventilation (HMV) either following an acute deterioration or when stable respiratory insufficiency is identified not only improves quality of life but extends meaningful survival. While HMV is associated with fewer hospital admissions and improved survival compared to oxygen therapy alone[1], there is a greater risk of complications and hospitalisations with invasive therapy compared to non-invasive ventilation[2]. A few years ago, the patterns and prevalence of HMV usage in Australia was undertaken[3]. At that time, the prevalence of HMV was at least [9.8] patients/100,000 population, although considerable variation in prevalence rates were seen, influenced by HMV centre location, size and experience. Major indications for HMV in Australia are neuromuscular disease (33%) and obesity hypoventilation syndrome (26%), with COPD and chest wall disorders accounting for around 10% of HMV prescriptions. By and large, most HMV patients are ventilated non-invasively using pressure preset modes of ventilation with an oronasal mask (62% oronasal vs 33% nasal). Ventilator-dependent patients made up 4.4% of the HMV population, about half of whom were also tracheostomised[3]. Although access to and use of non-invasive ventilation to manage chronic respiratory failure continues to increase in Australia due to greater knowledge, experience and funding, a number of challenges to successful and safe HMV remain. Equity of access to specialist HMV services for assessment and management is a problem for individuals in rural and remote areas of Australia. Funding of appropriate and timely HMV equipment also varies from state to state, despite generally uniform criteria for commencing therapy. However, advances in ventilator technology including autoadjusting settings and in-built ventilator software permitting remote access to detailed ventilation data are offering opportunities for more frequent monitoring and early troubleshooting for HMV clients irrespective of their geographical location. With increased recognition of the cost effectiveness of HMV, access to government funded equipment is improving, although funding of carers for many individuals remains limited, with reliance on family members to provide a majority of day to day care. Increasing use of continuous non-invasive ventilation for patients with progressive disorders requires clinicians and health care services to develop new skills and approaches to managing acute medical and surgical issues that arise with increasing longevity of this population. The role of high flow nasal cannula for patients with hypoxemic respiratory failure4 or chronic hypercapnia5 who are unable to tolerate non-invasive ventilation has yet to be fully explored in the Australia health setting.

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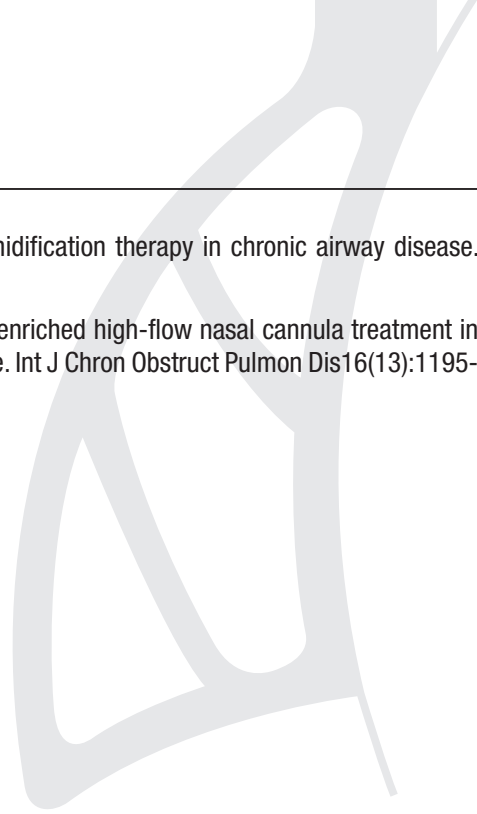
BEWARE OF DISTRESS

Menaldi Rasmin

ABSTRACT

Respiratory distress is a common condition that can be found in the Emergency Unit. Many of the patients having a pulmonary disease or problems such as pneumonia, bronchial asthma, COPD, bronchiectasis, TB, lung cancer and many more conditions. Respiratory distress is an increase and worsening respiratory effort that can be seen from clinical appearance. A study found that around 11% from Emergency encounters are respiratory distress cases. From this, 50% needs to be hospitalized, where 30% of it required intensive care and 15% needs the use of invasive ventilation, while 10% died prior to discharge. Dyspnea is the symptom that should be monitored earlier since this is the first symptom that will lead to respiratory distress. Dyspnea is a subjective experience of breathing discomfort that consists of qualitatively distinct sensation that varies in intensity (ATS Consensus Statement 1999). It is a complex symptom that warns a critical threat and the adaptive response. The frequency of 25 to 29 breaths per minute gives a mortality of 21% and, 27 breath per minute will lead to a cardiac arrest. The first priority in treating dyspnea patient is to identify and relief the pathologic process leading to the symptom. Common physiological situations can be the underlying processes such as neuromuscular, cardiovascular and of course, pulmonary problems. In some conditions, patient with dyspnea can fall into dyspnea crisis, a sustained and severe resting breathing discomfort that occurs in patients with advanced, often life-limiting illness and overwhelms the patient and caregivers' ability to achieve symptom relief. Since dyspnea usually put the patient into depression and anxiety, it will lead to a dyspnea crisis continue to respiratory distress andfailure.The treatment of dyspnea are prevention (e.g oxygen therapy, avoiding volume overload and nebulized bronchodilators), treating the underlying cause and palliation of distress.

HOW TO WEAN A PATIENT AS EARLY AS POSSIBLE

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ABSTRACT

Pathophysiology of weaning failure
Failure to wean has been attributed either to an imbalance between the load faced by the respiratory muscles and their neuromuscular competence or to an energy supply that is inadequate to meet the muscles energy demand.

1. Cardiovascular Dysfunction

Patients with underlying ventricular dysfunction may develop increases in PCWP and sometimes decrease in cardiac output upon removal of positive pressure ventilation. In patients with cardiac failure, high metabolic demands from overloaded ventilatory muscle loads coupled with compromised oxygen delivery during ventilatory support reductions may precipitate cardiac failure. Many factors have been implicated. (a) Increased preload (b) reduced left ventricular compliance (c) myocardial hypoxia (d) increased afterload.

During support or spontaneous breathing an increase in respiratory muscle workload as well as anxiety and sympathetic discharge result in an abrupt increase in oxygen and cardiac demand. The failing left ventricle is unable to respond normally and LVEDP rises causing alveolar edema. This in turn reduces lung compliance, increases airway resistance and worsens V/Q mismatch leading to hypoxemia.

3. Infection: Pneumonia can increase ventilatory muscle loads. Systemic metabolic effects of infection can directly impair respiratory muscle function as well as compromise O2 delivery.

4. Nutrition
5. Neurology: Critical illness polyneuropathy altered mental status
6. Fluid overload
7. Anxiety:

Assessment of patients who are able to sustain spontaneous breathing
1. Rapid breathing shallow index.
The frequency, tidal volume (f/VT) ratio, a measure of rapid shallow breathing introduced by Yang and Tobin in 1991, showed 95% of patients with a f/VT ratio higher than 105 failed the trial of weaning. Rapid shallow breathing indicates inspiratory muscle fatigue, response of the respiratory center to the dyspnea and anxiety.

2. Daily assessment of patients for weaning
In an elegant study Ely et al conducted a RCT in 300 patients receiving mechanical ventilation. Five simple weaning criteria were used daily for 2 hours spontaneous breathing. Ratio of PaO2/F102, PEEP < 5 cm H2O, f/VT < 105 BPM/L, airway reflexes and no vasopressors or sedation. They showed daily assessment reduced the duration of time spent on the ventilator.

Optimal method of Weaning

Esteban in 1995 prospectively evaluated 130 mechanically ventilated patients who met weaning criteria and failed 2-hr of spontaneous breathing. These patients were randomly allocated to be weaned by SIMV, PSV, T-Piece or once daily T-Piece. The rate of successful weaning was higher with a once daily trial of spontaneous breathing than with SIMV of PSV.

Esteban etal **(Esteban 1997 Spanish group)** reported the results of a RCT of spontaneously breathing via a T-Tube or pressure support. Among 484 patients, who had received mechanical ventilation for more than 48 hours, were assigned to undergo a two-hour trial of spontaneous breathing either by T-tube or by PSV of 7cm H2O. Of the 246 patients assigned to the T-tube group, 192 successfully completed the trial and were extubated. Thirty six of them required re-intubation within 48 hours. Of the 238 patients in the group receiving PSV, 205 were extubated and 38 of them required re-intubation within 48h. This shows ventilatory support can be successfully discontinued in two thirds of ventilated patients after a two-hour trial of spontaneous breathing

Reducing weaning duration by the implementation of a weaning protocol.

Saura P 1996 used a weaning protocol to predict the success of weaning. The protocol mainly consisted of, Pao2 > 60mm Hg and F102 < 0.4, PIMAX < - 20 cm H2O, RR< 35/min, VT > 5 ml/kg. Patients who did not meet 3 of the 4 criteria remained in assist-control made ventilation for 24h and then weaning criteria was reevaluated. Patients who met at least 3 of the 4 criteria underwent a weaning trial consisting of a 2-h period of spontaneous breathing on CPAP 5 cm H2O. Patients who tolerated the weaning trial were extubated.

Non-invasive mask ventilation (NIMV)

Nava et al in a study of COPD patients who had failed a spontaneous breathing trial and either returned them to mechanical ventilation (MV) or extubated them and placed them on NIMV. In the NIMV there was a significant return to MV. But, overall, there was less time using invasive MV.

Conclusion

1. A possible advantage of PSV over a T-piece trial of spontaneous breathing
2. A possible advantage to 30-min trial over 2h T-piece trial with respect to ICU and hospital stay.
3. Multiple dailies T-piece wean, or PSV may be superior to SIMV.
4. Weaning by protocol driven method is superior to physician driven method.

NEUROMUSCULAR DISEASE AND RESPIRATORY FAILURE

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ABSTRACT

Neuromuscular disease encompasses a broad range of disorders, each with its own underlying cause, pattern of weakness, rate of progression and prognosis. However, the pathway to the emergence of hypercapnic respiratory failure is similar. Respiratory muscle weakness impacts on lung volumes reducing vital capacity and, over the longer term, lung and chest wall compliance. As a consequence, the generation of tidal volume is reduced while respiratory rate increases. These changes are exacerbated during sleep, permitting an acute rise in carbon dioxide particularly during REM sleep. Over time with retention of bicarbonate, ventilatory responsiveness to CO2 worsens, promoting hypoventilation throughout sleep as well as during wakefulness. The presence of upper airway muscle weakness can contribute further to reduced ventilation during sleep. Although a number of daytime measures are used to monitor respiratory muscle weakness, no one measure has been shown to reliably predict nocturnal hypoventilation. Monitoring during sleep frequently involves nocturnal oximetry. However, in this population the degree of sleep hypoventilation can be significantly underestimated using oximetry alone. Transcutaneous carbon dioxide (TcCO2) monitoring has been shown to closely reflect CO2 levels and hence useful in identifying sleep hypoventilation. However, threshold values of TcCO2 that indicate clinically significant hypoventilation have yet to be identified.

APPROACH IMAGING OF IDIOPATHIC PULMONARY FIBROSIS

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ABSTRACT

Idiopathic pulmonary fibrosis (IPF) is defined as "a specific form of chronic, progressive fibrosing interstitial pneumonia of unknown cause, occurring primarily in older adults, limited to the lung, which lung tissue becomes damaged and scarred. The advent of new drug treatments has given hope for the future and raised the profile of IPF.

It is important to know IPF is a clinical diagnosis and usual interstitial pneumonia (UIP) is a radio pathological pattern of disease. IPF is diagnosed by identification of a pattern of UIP on the basis of radiological or histological criteria in patients without evidence of an alternative cause. The correct use of clinical-pathological and radiological terminology is essential to avoid confusion.

A high-resolution computed tomography (HRCT) scan is an important tool to evaluate IPF. Several abnormalities can be observed using this method, such as ground-glass opacities, consolidation, reticulation, and honeycombing. The extent of fibrosis may also be measured by evaluating the combination of reticulation and honeycombing.

A confident diagnosis of IPF can be made in the correct clinical context when CT imaging shows a pattern of typical or probable UIP. Importantly, a confident diagnosis of IPF were made based on clinical and radiological pattern in approximately two-thirds of cases. International management guidelines highlight the critical role of radiology as part of a multidisciplinary team (MDT) approach in reaching an accurate and early diagnosis of IPF.

Keywords
Idiopathic pulmonary fibrosis, usual interstitial pneumonia, HRCT, multidisciplinary team

CARDIOVASCULAR COMPLICATION OF SEPSIS DUE TO LRTI

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ABSTRACT

More than 1.5 million unique adults will be hospitalized in the United States each year due to community-acquired pneumonia (CAP), and approximately 100,000 adults will die during their hospitalization. Hospitalization for CAP is associated with increased short-term and long-term risk of cardiovascular disease. One year after a hospitalization due to CAP, death will occur in nearly 1 of 3 adults. Few of these patients die of sepsis. Acute myocardial infarction (AMI) occurs in 4 – 7 % of patients admitted to hospital with CAP. Cardiovascular complications including AMI, congestive heart failure and cardiac arrhythmias occur in up to 27% of patients. Cardiovascular complications are related to the severity of CAP, specific bacterial pathogens, and the presence of underlying cardiovascular disease. Intrahospital cardiac complications, age, and Pneumonia Severity Index are significantly associated with overall mortality when patients are followed for up to five years.

There are several mechanisms that have been identified with the risk of cardiovascular complications. CAP is associated with platelet activation and a pro-coagulant state. Streptococcus pneumoniae, in particular, has been shown to Invade the myocardium and form microlesions, induce ion flow disturbances and electrophysiological abnormalities, kill cardiomyocytes in a pneumolysin-dependent manner, generate enlargement and instability of atherosclerotic plaques, provoke necroptosis in cardiomyocytes and macrophages infiltrating the heart, promote platelet activation and, after antibiotic treatment, induce heart scarring. Observational studies have suggested that chronic statin therapy taken before the onset of pneumonia, may reduce mortality in hospitalized pneumonia patients. Angiotension II receptor blockers, angiotensin converting enzyme receptor inhibitors but not beta-blockers have also been associated with reduced mortality in these pneumonia patients. Concurrent aspirin use has also been associated with a reduction in cardiovascular events. None of these agents, however, have been studied in large scale, prospective randomized controlled trials. Antipneumococcal vaccination may be the best approach to prevent cardiac complications associated with pneumonia simply be reducing the risk of pneumonia in general.

MICROBIOM: RISK FACTOR ON RESPIRATORY FAILURE

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ABSTRACT

Acute respiratory distress syndrome (ARDS) is a severe lung inflammation disorder, that was common among severe clinically ill patients, especially in ICU patients. Sepsis is the main cause of this disease. The cellular level, there was a disturbance of epithelial on capillary vascular and impact on fluid leakage into the pulmonary parenchyma (Gonzales et al, 2015).

Most of ARDS were caused by opportunistic bacterial infection.Dickson (2016) has stated the changes of lung microbiome in respiratory tract of were enriched with gut bacteria, among ARDS's patients. This phenomenon was also identified in murine model of sepsis. TNF-alpha that served as an indicator for ARDS was dominant among ARDS patients. Kelly et al (2016) show the similar picture, among patients with ventilator, there were changed of their lung microbiota, from the more diversity, to single taxon or low diversity.

It was a question about the human immune system, to be designed to control microorganisms OR was controlled by microorganisms. Critically illnesses were rapidly changed to significant dysbiosis and many taxons of health promoting bacteria were depleted. An intervention by introducing microbiota in patients with severe traumatic brain injury, can improve the pattern of immune status, decrease the nosocomial infection and shortened the hospital stay (Tan et al, 2011). The patients with intervention were also have higher concentration of IFNy and lower IL-4 as an effector cell and IL-10 as an anti inflammatory factor. It means that the immune power is increasing.

Various studies have shown that the total number and composition of intestinal microbes shift in old flies. These changes are associated with mis-regulation of intestinal immune signaling and a breakdown in intestinal compartmentalization (Li et al, 2016). The study of Thevaranjan (2017) maintained under germ-free conditions,mice do not display an age-related increasein circulating pro-inflammatory cytokine levels. It showed that the microbiota has a role in systemic immune responses.

According to the presenting of microbiota in gut space, is it an infection or not. By the definition, an infectious disease is an entrance of microbe into internal body site, multiply and impact on host responses, in both of cellular and interleukin.The lamina propria layer that located under the epithelial cell, is an immune rich layer with macrophages, T cells, dendritic cells (DCs), plasma cells and innate lymphoid cells (ILCs). There is a pattern recognition receptor (PRR) to recognize the bacterial antigen. The increasing of bacterial microbiota,will increase the PPR, and more cellular community in intestinal wall. The PRR and also the other intestinal cellular, were also able to spread systemically and work as an immune components (MGS, 2012). The dendritic cell in gut wall, have unsuspected role in collecting the antigen in both of intestinal lumen and circulating antigens. In germ free animal, the cecal size was decrease (Syed et al, 1970).

The depleting or dysbiosis would be caused by antimicrobial effect or other affiliated disease. The impact

of immune responds due to the dysbiosis will aggravated theinfection, included the respiratory failure, such as ARDS caused by infection.

Conclusion: Respiratory failure, such as ARDS was direct or indirectly associated with microbiome, that has an important role in arrangement of immune system, in both of locally and systemically. The depleted of gut flora will impact on smaller size of cecal due to the depleted of other cellular components that mostly immune materials, and will also decrease the defend of the body, included the pulmonary system.

Keywords: microbiome, dysbiosis, ARDS, respiratory failure

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COMPLICATION OF NONINVASIVE VENTILATION

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ABSTRACT

Non-invasive ventilation (NIV) has become a standard of care in both hypercapnic and non-hypercapnic acute respiratory failure. However, patient tolerance to the technique is a critical factor determining its success in avoiding endotracheal intubation

Drawbacks of NIV are mainly linked to 3 important issues:
1) Patient-ventilator dys-sinchrony
2) Compliance with the interfaces

Patient-ventilator dys-sinchrony

Optimal patient–ventilator synchrony can prove very difficult to achieve, especially during NIV, due to the presence of leaks at the patient-mask interface which can interfere with various aspects of ventilator function . This interference can increase the risk of asynchrony, which in turn leads to an increase in the work of breathing and patient discomfort .

A multicenter study found that patient– ventilator asynchrony is common in patients receiving NIV for acute respiratory failure. The authors found that that leaks played a major role in generating patient–ventilator asynchrony and discomfort clinical setting.

Manufacturers often propose new modes, but scientific evidence proving their effectiveness and clinical benefit is often lacking. Neurally adjusted ventilator assist (NAVA) is designed to enhance patient-ventilator synchrony. NAVA uses an esophageal catheter to detect diaphragmatic activity and thus the patient's effort regulating the amount of delivered pressure. Triggering and cycling of the ventilator are activated by NAVA. It decreases ineffective efforts (trigger asynchrony) and premature and delayed cycling (cycle asynchrony) compared with pressure-controlled flow-cycled ventilation (ie, PSV), thereby improving patient ventilator synchrony. Its role seems promising during helmet ventilation.

Compliance with interfaces

The perfect NIV interface does not exist, but the choice of an adequate interface should be tailored to the patient's characteristics and influenced by ventilator setting and the patient's underlying type of respiratory failure. A good seal to prevent leaks, and patient comfort with the prevention of drawbacks and complications should be the major goals for clinicians. Fitting the mask to the patient rather than trying to make the patient fit the mask is mandatory, but this is only possible with a large range of interfaces and sizes. The larger the availability of interfaces and sizes, the higher the probability of success in fitting the interface to the patient. In the acute setting, the oronasal interface (covering the surface around the nose and the mouth) is the most commonly used. Total full-face mask (TFMs; covering the entire anterior surface of the face, including the mouth, eyes, and nose) and helmet (a transparent hood and soft polyvinyl chloride or silicon collar that includes the neck and whole head) may also be used in the critical care setting. Nasal masks, oronasal masks, and TFMs are available in vented and nonvented versions. Vented mask have some holes or slots in the frame or on the swivel elbow that allow CO_2 diffusion. CO_2 levels may increase in vented masks because of CO_2 rebreathing. However, as recently underlined, a proper setting and larger leaks from

the new vented system embedded in the interface reduce the likelihood of CO_2 rebreathing.The vented configuration of oronasal masks and TFMs is always equipped with an anti-asphyxia valve with automatic opening to prevent rebreathing in case of a pressure failure or when airway pressure decreases to less than 2 to 3 cm H_2O.Nonvented masks are completely closed and require the use of a double-limb or single-limb circuit with an expiratory valve. A recent study found that effective dead space in nonvented interfaces with large volumes is not related to the internal gas volume of the interface, suggesting that this internal volume should not be considered as a limiting factor for their efficacy during noninvasive ventilation. Compared with nasal masks, oronasal interfaces have the potential advantage of fewer air leaks and greater stability in the delivered mean airway pressure, especially in the acute setting or during sleep. In the acute setting, less patient cooperation is required during NIV. For these reasons its use should be preferred to nasal interfaces during the acute phase of respiratory failure; when patients are intensively dyspneic and, generally, in open-mouth breathers. The TFM avoids the nasal bridge, creating an effective seal around the less pressure-sensitive perimeter of the face, limiting the risk of deleterious cutaneous side effects. The TFM mask also has the advantage of rapid and easy application, and it is a valid alternative for patients who are unable to obtain a good seal with other masks. It can also be used in the case of nasal bridge skin breakdown and facial irregularities. Its use has some limitations in claustrophobic patients. There is no clear evidence yet on the advantages in terms of effectiveness and compliance of TFM compared with other conventional oronasal masks. However, in patients with hypercapnic ARF, for whom escalation to intubation is deemed inappropriate, switching to a total face mask has been proposed as a last-resort therapy when face mask–delivered NIV has already failed to reverse ARF. This strategy has been found to provide prolonged periods of continuous NIV while preventing facial pressure sores. Moreover, it allows a clear and unrestricted view, as with the helmet. Helmet interfaces were originally used to deliver a precise oxygen concentration during hyperbaric oxygen therapy. The United States Food and Drug Administration has not approved any of the available helmets, but helmets have been approved in some other countries. When using a helmet with a CPAP generator, a minimum flow of 40 L/min is mandatory to avoid CO_2 rebreathing. For the same reason, CPAP alone should not be used with ICU ventilators in the nonvented configuration because the flow that is generated is too low to wash CO_2.

Recent engineering improvements gave helmets more comfortable seals, better seal against leaks, and better patient-ventilator interaction. A new type of full-face mask, provided with nasal and oral ports that can be used in ongoing endoscopic procedures in case of respiratory failure without interrupting the procedure, has recently been introduced as a prototype. This mask is able to support ventilation in a few seconds because it is made of 2 symmetric parts that can be divided in order to place it in on the patient during the procedure, even if an endoscopic probe is already inserted.

Suggesting lectures
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DOI 10.1007/s00134-009-1416-5

PULMONARY EMBOLISM THE ROLE OF GREAT SAPHENOUS VEIN DILATATION

Ismoyo Sunu

ABSTRACT

Great Saphenous Vein (GSV) dilatation is one of chronic venous insufficiency diseases that often associated with varicose occurrence. There is ample evidence that GSV ablation can eliminate varicose veins. The prevalence of chronic venous insufficiency by Framingham Score (1988) is twice greater than coronary heart disease and the prevalence of varicose veins in the Middle East and Europe are 18%. The results of Harapan Kita Heart Hospital's registry show the prevalence of varicose veins by 10% but we know that these diseases include non-life-threatening illnesses. Assessment of PJNHK registry results 2015-2016 on chronic venous insufficiency disease showed that the width of GSV diameter hence also increase the chance of pulmonary embolism on the interpretation of pulmonary perfusion scanning. Until now there has been no study linking GSV with non-thrombotic dilatation with pulmonary embolism event. This presentation has a goal to expect that pulmonary embolism not only comes from deep venous thrombosis but needs to be assessed through studies of GSV dilatationbetween pulmonary embolism. It is hoped that in the future GSV ablation is needed to prevent life-threatening pulmonary embolism.

SATURDAY, 21ˢᵗ JULY 2018

INITIAL ASSESSMENT AND VENTILATORY STRATEGY FOR ACUTE RESPIRATORY FAILURE IN CHILDREN

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ABSTRACT

Managing a child who is in acute respiratory failure (ARF) is challenging for primary care pediatricians. ARF is the most common cause of cardiac arrest in children. Failure to recognize and manage respiratory failure can result in patient death or longterm disability. The prompt recognition of respiratory failure requires an index of suspicion when presented with the signs and symptoms of acute respiratory insufficiency such as decreased level of consciousness, slow/shallow breathing, or increased respiratory drive. The adequacy of breathing systematically evaluated by history, physical examination, and measurements of gas exchange. A brief history should identify any underlying diseases, complication and the extent and rate of change in mental status and breathing. An efficient approach to the examination is to begin with the "30-second cardiopulmonary assessment".

The first priorities in treating ARF are to assure adequate gas exchange and circulation (the ABCs of cardiopulmonary resuscitation). Oxygen should be delivered to maintain the arterial oxygen saturation above 95%. If ventilation is or appears to be inadequate, breathing should be initiated with a bag-mask system with added oxygen. Mechanical ventilation (MV) is a lifesaving therapy, allowing support of patient with ARF with the objective of improving gas exchange and decreasing work of breathing. MV consists of a pressurized volume of gas delivered by either an invasive or non invasive interface. MV is challenging in children because of heterogeneity of this population in terms of age, weight and pathophysiology.

Keywords: acute respiratory failure, ventilatory strategy, children

NON INVASIVE VENTILATIONPADAOBSTRUCTIVE SLEEP APNEA SYNDROME

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ABSTRACT

Obstructive sleep apnea syndrome (OSAS) is known as a disease in children that can interfere the growth process to reach the genetic potential due to its complication. The diagnosis and prevention of OSAS complications need to be known and well managed. The major risk factors for OSAS in children are adenoid or tonsilar hypertrophy and several other risk factors such as facial disproportion and obesity. The management of OSAS is the administration of intranasal corticosteroid or tonsiloadenoidectomy (TA). In certain conditions, tonsiloadenoidectomy may not be as favorable as expected in terms of facial disproportion and obesity with or without hypertrophy adenoid. In this case other management is required with non-invasive ventilation (NIV). Continuous positive airway pressure (CPAP) is considered the second line of treatment in children with unresolved OSAS after TA. CPAP utilization is to prevent the occurrence of airway obstruction that can lead to hypoxia, reducing the respiratory muscle burden, and improving the lung function especially for the gas exchange process. Two types of CPAP are auto-CPAP and manual. On auto-CPAP, machines can independently adjust incoming airflow accordance with the degree of obstruction occur, while the manual cannot adjust to the degree of obstruction. CPAP utilization has no absolute contraindication but there are some relative contraindication conditions such as general or unstable awareness, unable to maintain the airway, obstruction, and unstable hemodynamic. Some of the complications of CPAP are irritation on face, conjunctivitis, and facial changes.

Key words: NIV, OSAS, children

PITFALLS IN NEONATES RESPIRATORY FAILURE

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ABSTRACT

Respiratory failure is the most common problem found in the preterm and term neonates admitted to neonatal intensive care units (NICU). In preterm neonates, the most common cause of respiratory failure is respiratory distress syndrome (RDS) due to surfactant deficiency. In term neonates, respiratory failure usually caused by meconium aspiration syndrome, neonatal sepsis, pulmonary hypoplasia. Persistent pulmonary hypertension of newborn (PPHN), with or without parenchymal lung disease, can cause severe hypoxemic respiratory failure in preterm and term neonates.

The methods treatment of respiratory failure in neonates is vary, depend on the causeand severity of respiratory failure, including antenatal steroids for the prevention of respiratory distress syndrome, exogenous surfactant administration, high frequency ventilation, continuous positive airway pressure,extracorporeal membrane oxygenation.

Antenatal steroids given for fetal lung maturation and exogenous surfactant administration have dramatically reduced the mortality of neonates with respiratory distress syndrome.

Key words: *preterm and term neonates, respiratory distress syndrome, respiratory failure,*

SEPSIS AND RESPIRATORY FAILURE

Ronald F. Grossman

ABSTRACT

Sepsis is defined as an infection complicated by life-threatening organ dysfunction due to a dysregulated host response. Organ dysfunction can be represented by an increase in the Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score of 2 points or more.Septic shock is defined as a subset of sepsis in which particularly profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone. A vasopressor requirement to maintain a mean arterial pressure of 65 mm Hg or greater and serum lactate level greater than 2 mmol/L (>18 mg/dL) in the absence of hypovolemia is usual. The incidence of sepsis is rising but the mortality rate is decreasing. Culture-negative sepsis is associated with a higher mortality rate compared to culture-positive sepsis. The commonest reasons for invasive mechanical ventilation in this patient population cited by physicians are profound hypoxemia, tachypnea, hypotension, requirement for vasopressors and alterations of consciousness. Patients presenting with the combination of acute respiratory failure and severe sepsis have a significantly worse prognosis compared to patients presenting with one or none of these features.

The antimicrobial treatment of severe sepsis involves several basic principles. Effective antibiotic therapy must be administered as quickly as possible. Empiric broad-spectrum therapy with one or more antimicrobials for patients presenting with sepsis or septic shock should be started to cover all likely pathogens (including bacterial and potentially fungal or viral coverage often depending on the initial site of infection). Empiric antimicrobial therapy should be narrowed once pathogen identification and sensitivities are established and/or adequate clinical improvement is noted. Dosing strategies of antimicrobials should be optimized based on accepted PK/PD principles and specific drug properties. Empiric combination therapy (using at least two antibiotics of different antimicrobial classes) aimed at the most likely bacterial pathogen(s) for the initial management of septic shock is necessary. In contrast, combination therapy should not be routinely used for ongoing treatment of most other serious infections, including bacteremia and sepsis without shock. Antimicrobial treatment duration of 7–10 days is adequate for most serious infections associated with sepsis and septic shock. Measurement of procalcitonin levels can be used to support shortening the duration of antimicrobial therapy in sepsis patients. Adjunctive therapy with statins and corticosteroids is of limited value.

MEDIASTINAL TUMOR AND RESPIRATORY FAILURE

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ABSTRACT

Respiratory failure is defined as a syndrome in which the respiratory system meets failure in its gas exchange functions. Respiratory failure can be classified into hypoxemic or hypercapnic and acute or chronic.

Mediastinum is a space within the thoracic cavity surrounded by lung, vertebrae and sternum. Mediastinal neoplasm may arise from any tissues within mediastinum and many types of tumors may have different characteristics but each has potential effect in causing respiratory failure.

Mediastinal tumors can cause respiratory failure that occur in many ways. This respiratory failure may be caused by direct obstruction of airways and or indirect cause e.g. paralysis of respiratory muscles due to nerve infiltration or tumor characteristics like thymoma with myasthenia gravis.

According to Surabaya experiences, we found so many cases came to see us in a late stage and worse condition and difficult to treat. In other hand, we have successfully treated some thymoma with respiratory failure including non thymomatous with myasthenia gravis since year of 2000 with good results. Understanding and meticulous diagnostic is very important to prevent and treat respiratory failure due to mediastinal tumors.

Keywords: *mediastinal tumor, respiratory failure, thymoma, non thymomatous thymoma*

MANAGEMENT OF RECURRENT COUGH IN CHILDREN

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ABSTRACT

Cough is one of most common symptoms in children who come to the physicians. Cough can be classified based on time frame (ie, duration of cough), quality (eg, dry or wet,brassy, or staccato), or suggested etiology (ie, specific and nonspecific). Most common of cough is acute cough, which is usually caused by viral self-limiting upper acute respiratory infection. Chronic or recurrent cough may represent the more serious diseases and make the parents' concerns.

Chronic cough in children is cough persisting more than 4 weeks, according to the US and Australian-New Zealand guidelines, or more than 8 weeks, according to the UK guidelines.In clinical setting, chronic or recurrent cough may be difficult to be defined by parents, so that Indonesian Pediatrics Society also use the term of recurrent chronic cough that is cough that lasts for 2 weeks and/or cough that repeats at least 3 episodes in 3 consecutive months with / without respiratory or other non-respiratory symptoms.

The causes of chronic/recurrent cough in children vary depending on age. Chronic cough in children can be classified into 3 etiological groups: Normal or expected cough (the cause is known, so the cough is considered expected and no specific studies are required); specific cough (cough that occurs with signs and symptoms suggesting a specific diagnosis that has been reached after thor- ough examination) and non-specific cough (syndromes that present with predominantly dry isolated cough, with no signs or symptoms suggestive of disease)

Chronic cough should be treated after a thorough clinical investigation to eliminate the causative agent. Irrespective of the cause of cough, particular attention to tobacco smoke exposure as well as parental expectations and concerns are advised. Chronic cough due to asthmarequires treatment with bronchodilators and, depending on classification, with inhaled corticosteroids.Protracted bacterial bronchitis needs long-termtreatment (between 2 and 6 weeks) with amoxicillin–clavulanateor clarithromycin.

If the recurrent cough has a moderate impact, but there is no underlying disease and the child is healthy, a period of observation is recommended before diagnostic tests or treatment are initiated, with a follow-up examination of the child after 6–8 weeks. If a decision is taken to carry out a trial treatment, the duration should be empiric and based on the recommendations of experts. For reducing the symptoms, mucoactive is a type of drug that can change the components of mucus viscoelasticity to help airway clearance so that no obstruction occurs due to abnormal mucus secretion. The study found that combination of erdostein and antibiotics was more effective than the combination of antibiotics and placebo in relieving cough symptoms in acute bacterial respiratory infections. Cough has a role as a protective reflex, therefore cough reflex suppression should not be done without identifying and managing the etiology.Studies also suggest that antitussive is not more effective than placebo for acute cough symptoms. The use of codeine is prohibited in the management of cough in children because of the risk of serious adverse effects, most notably the breathing disorder. In patients with asthma, antitussive administration is contraindicated. As a summary: Cough is part of the respiratory defense mechanism, along with mucocilliary clearance. If the child has a chronic/recurrent cough, specific symptoms and markers for specific diseases should be investigated so

that the definitive diagnosis can be established and appropriate management can be performed. Cough medication in children should be based on the effectiveness and safety of drugs.

THE LATEST STUDY REGARDING THE ROLE OF MUCOACTIVE TETRDYNAMIC ON COPD EXCERBATION

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ABSTRACT

Background: Oxidative stress contributes to chronic obstructive pulmonary disease (COPD) exacerbations and antioxidants can decrease exacerbation rates, although we lack data about the effect of such drugs on exacerbation duration. **Methods :** The RESTORE (Reducing Exacerbations and Symptoms by Treatment with ORal Erdosteine in COPD) study was a prospective randomised, double-blind, placebo-controlled study, enrolling patients aged 40–80 years with Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage II/III. Patients received erdosteine 300 mg twice daily or placebo added to usual COPD therapy for 12 months. The primary outcome was the number of acute exacerbations during the study. **Result:** In the pre-specified intention-to-treat population of 445 patients (74% male; mean age 64.8 years, forced expiratory volume in 1 second 51.8% predicted), erdosteine reduced the exacerbation rate by 19.4% (0.91 versus 1.13 exacerbations per patient per year for erdosteine and placebo, respectively; p=0.01), due to an effect on mild events; the reduction in the rate of mild exacerbations was 57.1% (0.23 versus 0.54 exacerbations per patient per year for erdosteine and placebo, respectively; p=0.002). No significant difference was observed in the rate of moderate and severe exacerbations (0.68 versus 0.59 exacerbations per patient per year for erdosteine and placebo, respectively; p=0.054) despite a trend in favour of the comparison group. Erdosteine decreased the exacerbation duration irrespective of event severity byc24.6% (9.55 versus 12.63 days for erdosteine and placebo, respectively; p=0.023). Erdosteine significantly improved subject and physician subjective severity scores (p=0.022 and p=0.048, respectively), and reduced the use of reliever medication (p<0.001), but did not affect the St George's Respiratory Questionnaire score or the time to first exacerbation. **Conclusion**, in patients with COPD, erdosteine – with its tetradynamic mucoactive properties (mucomodulator, bacterial anti-adhesion, antioxidant, anti-inflammation) – can reduce both the rate and duration of exacerbations. The percentage of patients with adverse events was similar in both the placebo and erdosteine treatment groups, suggesting that erdosteine is safe and effective.

Key words: COPD, Exacerbation, Erdostein, tetradynamic mucoactive.

Reference:

Dal Negro RW, Wedzicha JA, Iversen M, et al. Effect of erdosteine on the rate and duration of COPD exacerbations: the RESTORE study. Eur Respir J 2017;50:1700711.

MAXIMIZING THE TREATMENT FOR COPD EXACERBATION

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ABSTRACT

Chronic respiratory accounts for a large proportion of global mortality and COPD is one of them. It is estimated in 2030 COPD will be third biggest global killer in 2030. Under diagnosis and misdiagnosis is still a problem in COPD. WHO Global Action Plan for reduction of morbidity, mortality and disability due to non-communicable diseases such as COPD includes improvement in diagnostic services. Spirometry is important for the correct diagnosis of COPD and lack of routine spirometry is a major cause for misdiagnosis.

Based on GOLD guideline, the goals of COPD treatment is to reduce symptoms and reduce risk. Grouping of the patients based on their symptoms and exacerbation history is used to determine the appropriate treatment. Bronchodilators (such as LABA, LAMA, etc) are the cornerstone of COPD treatment. In accordance with GOLD, there is considerable evidence and guidance to support use of the combination of a LAMA and a LABA in COPD.

Studies showed that combination LABA+LAMA provide greater improvement compared with monotherapy or placebo. In FLAME study showed that fixed dosed combination (FDC) LABA+LAMA demonstrated superiority versus LABA/ICS for of all exacerbations.

FDC offer the potential of improved convenience and compliance over use of separate inhalers. ICS used is associated with increased risk of pneumonia. GOLD do not provide guidance regarding how to escalate/deescalate treatment. However few studies provide evidence for the effective switching and removal of ICS. In 2017, The International Primary Care Respiratory Group (IPCRG) algorithm explain about in whom and how to withdraw ICS.

Key word : COPD, exacerbation, LABA, LAMA, LABA/ICS, GOLD

CARDIOVASCULAR APPROACH IN CHRONIC RESPIRATORY FAILURE

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21 July 2018

ABSTRACT

Respiratory failure is still an important complication of chronic obstructive pulmonary disease (COPD) and hospitalisation with an acute episode being a poor prognostic marker. It is a common and important event, which is frequently associated with severeexacerbations of COPD.Commonly respiratory failure results from disturbances of gas exchange due to impairments in either oxygenation, or elimination of carbon dioxide, or both (Roussos et al 2003). For clinical routine purposes, respiratory failure is usually defined by an arterial oxygen tension (PaO2) of less than 60 mmHg and/or an arterial carbon dioxide tension (PaCO2) greater than 45 mmHg.

Pulmonary hypertension (PH), defined as an elevated meanpulmonary arterial pressure (mPAP) ≥25mmHg, is a commoncomplication of chronic lung disease (CLD), including COPD.The increase in pulmonaryartery pressures is often mild to moderate. However, 5–10% ofpatients with advanced COPD may suffer from severe pulmonaryhypertension and present with a progressively downhill clinicalcourse because of right heart failure added to ventilatory handicap.

The cause of pulmonary hypertension in COPD is generally assumed to behypoxic pulmonary vasoconstriction leading to permanent medialhypertrophy. However, recent pathologic studies point rather atextensive remodeling of all layers of the pulmonary arterial walls.PHoften progresses to right heart failure (RHF), with initialcompensatory right ventricular (RV) hypertrophy becomingoverwhelmed by increased systolic requirements, whilst leftventricular (LV) systolic function remains preserved. Theterm "corpulmonale" has been used to describe this form ofRHFand hypertrophy. It is a progressive condition, associatedwith increased mortality in CLD.

Right ventricular dysfunction arises in chronic lung disease when chronic hypoxemia anddisruption of pulmonary vascular beds contribute to increase ventricular afterload, and is generallydefined by hypertrophy with preserved myocardial contractility and cardiac output. Although theexact prevalence is unknown, right ventricular hypertrophy appears to be a common complicationof chronic lung disease, and more frequently complicates advanced lung disease. Right ventricularfailure is rare, except during acute exacerbations of chronic lung disease or when multiple comorbiditiesare present. Treatment is targeted at correcting hypoxia and improving pulmonary gasexchange and mechanics. There are presently no convincing data to support the use of pulmonaryhypertension-specific therapies in patients with right ventricular dysfunction secondary to chroniclung disease.

The management of RV failure should always take intoaccount the origin of and setting in which RV failure occurs.Specific treatment goals include optimization of preload,afterload, and contractility. Maintenance of sinus rhythm andatrioventricular synchrony is especially important in RVfailure because atrial fibrillation and high-grade atrioventricularblock may have profound hemodynamic consequences.Ventricular interdependence also is an important concept toconsider when tailoring therapy. Excessive volume loadingmay increase pericardial constraint and decrease LV preload and

cardiac output through the mechanism of ventricularinterdependence. Alternatively, hypovolemia may decreaseRV preload and cardiac output. In acute RV failure, everyeffort should be made to avoid hypotension, which may leadto a vicious cycle of RV ischemia and further hypotension.

The management of isolated acute right heart failure remains more of an art than a science in the absence of robustrandomiseddata. In addition to treating the specific cause, RV preload optimisation, the use of selective pulmonary vasodilators, RV inotropic support and temporary mechanical circulatory device therapy form integral components of a comprehensive strategy to support the failing right heart.

RESPIRATORY FAILURE IN UNCONTROLLED ASTHMATIC PATIENT

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ABSTRACT

Not all patients with "difficult-to-control" asthma have "severe asthma". Many of them have either an incorrect diagnosis, or mild–moderate asthma with unrecognised aggravating factors, or are non-compliant with prescribed therapy. For a diagnosis of severe asthma, it is necessary to confirm the diagnosis of asthma, to evaluate and treat endogenous and exogenous aggravating factors, and to closely follow the patient for ≥6 months.

Severe asthma is a heterogeneous condition with different phenotypes. Defining clinical phenotypes is necessary to improve understanding of underlying mechanisms, to help guide current treatment and to provide clues for novel therapeutic interventions. Despite intensive multi-drug treatment with high-dose inhaled and oral corticosteroids, many patients with severe asthma remain uncontrolled. There is an urgent need for new, more-effective treatments.

This case describes a patients with a severe near.fatalsavere asthma. Fatal and near-fatal asthma represent the most extreme manifestations of severe asthma exacerbations. Hospitalisation and emergency visits during the previous year and psychosocialfactors seem to be most important risk factors. Lower socio-economic status, less access to medical care, ethnic origin, depression, denial, psychiatric problems and illicit drug abuse are all recognised determinants for a lethal exacerbation. The pathophysiological features associatedwith frequent or (near-) fatal exacerbations in Asthma are largely unknown, but studies suggest hat these patients have a decreased perception of dyspnoea, increased airway responsiveness, and evidence of air trapping and early airway closure.

Possible different clinical paths to deal with this patients will be described including invasive mechanical ventilation

Suggesting lectures
Bel EH Breathe | 2006 ; 3 | No 2

Global Strategy for Asthma Management and Prevention (2018 update)https://ginasthma.org/2018-gina-report-global-strategy-for-asthma-management-and-prevention/

CHRONIC PULMONARY PROBLEM : UNCONTROLED ASTHMA IN REHABILITATION PRESPECTIVE

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ABSTRACT

Pulmonary rehabilitation (PR) is a non pharmacological treatment for chronic pulmonary problem, especially chronic obstructive disease. The main objective is to eliminate or reduce its symptoms. PR was designed to improve functional capacity and quality of life, besides relieving symptoms. A PR program which trains the ambulatory muscles and to improve the symptom of dyspnea both has the most powerful evidence base (1A), which is highly recommended.

Sahin H and Naz I in their studies, compared the effect of pulmonary rehabilitation in patients with uncontrolled and partially controlled asthma. Uncontrolled asthma was recognized as asthma with Asthma Control Test (ACT) $\leq$ 19. It is characterized by activity limitation, daytime shortness of breath, awakening of the night, and increased use of asthma control drugs. PR programs is designed individually, they included dyspnea control with relaxation, breathing exercises, upper and lower extremity exercises, and aerobics. There is significant symptom improvement in both groups, with higher ACT score in uncontrolled asthma.

We mentioned several studies based on COPD patients as its role model for PR.
Nusdwinuringtyas N and Islamadina B conducted pulmonary rehabilitation study in patients with COPD. It obtained the total SGRQ score was 13,5%, while Paul W Jones mentioned total MCID SGRQ score on drug administration alone is only 4%.

Unfortunately, six-minute walk test is hardly applicable for uncontrolled asthma patients as fears become congested during the test. Therefore, four-meter walk test could be an option.

In a study conducted by Nusdwinuringtas using patients with COPD that were mostly classified as group D, all patients were able to perform four-meter walk test. As the compatibility between six-minute walk test and four-meter walk test has been proven.

Conclusion : Uncontrolled asthma is not contraindicated for pulmonary rehabilitation. Controlling Chronic Obstructive Pulmonary Disease should be accompanied with pulmonary rehabilitation program. Functional capacity evaluation could be measured with four-meter walk test and quality of life could be evaluated by SGRQ.

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CURRENT CARE TO IMPROVE THE OUTCOME OF COPD: ADDRESSING THE TREATABLE TRAIT

Celeste Mae Campomanes

ABSTRACT

COPD prevalence is high in Asia and will continue to rise due to not only the increase in smoking prevalence, but increase in air pollution though indoor biomass fuel and outdoor pollution as well as other risk factors like occupational exposure and prior conditions like PTB and asthma. The greatest burden of COPD is highest in Asia where the age-adjusted mortality is highest in the world. Aside from this, COPD imposes a significant clinical burden on patients by increasing their symptoms of breathlessness, reduced mobility and increasing their probability of exacerbations. It is recognized that exacerbations accelerate the disease progression, lung function decline, and morbidity and mortality. Co-morbidities like cardiovascular diseases, osteoporosis, anxiety and depression, GERD, sleep apnea, other metabolic disturbances and malnutrition, increase the burden of care among our COPD patients.

The COPD treatment paradigm is rapidly evolving with the numerous landmark trials being conducted to address the goals of management in the heterogeneous COPD population, specifically reduction in symptoms and reduction in risk for exacerbation, mortality and disease progression. There is strong evidence supporting the use of maximum bronchodilatation (LAMA/LABA) therapy for symptomatic COPD patients.

Exacerbations are strongly linked to disease progression and it has been established that the strongest predictor of future exacerbations is a history of exacerbations as demonstrated in the ECLIPSE study. Thus, for these patients who remain symptomatic with increased risk for exacerbations while on their maintenance treatment, an ICS containing regimen like triple therapy (ICS-LABA+ LAMA) may be appropriate. The established benefits of ICS-containing therapy need to be balanced with the risks, in particular pneumonia.

Although bronchodilation remains the cornerstone of treatment for stable COPD patients additional pharmacologic and non-pharmacologic modalities may be necessary specially for the frequent exacerbators, the patient with multiple comorbidities, the physically frail, and those with features of asthma. Special attention must be given to the holistic management of COPD management to better reduce symptoms and reduce risks for exacerbations by concurrently addressing the comorbidities, nutritional status and muscle deconditioning among our COPD patients.

FROM INFECTION TO RESPIRATORY FAILURE

Ronald F. Grossman

ABSTRACT

Severe community-acquired pneumonia (SCAP) has been defined as the presence of severe acute respiratory failure (ARF) and needing invasive mechanical ventilation (IMV) and/orseptic shock with organ system dysfunction. Nearly 5% of patients with severe CAP admitted to hospital will require invasive mechanical ventilation. Respiratory acidosis, poor gas exchange, high CURB-65 score, and the presence of pleural effusion, renal failure and septic shock, all predict the need for IMV. Streptococcus pneumoniae is the most important pathogen associated with SCAP. Serotypes associated with thicker surface capsules (serotypes 3, 6A, 6B, 19F, 23F) are more often associated with septic shock, necrotizing pneumonia, need for IMV and mortality. Serotypes 3 and 19A are more likely to be associated with bilateral lung infiltrates. Combination therapy (macrolide or fluoroquinolone + β-lactam) is associated with improved outcomes in critically ill patients particularly demonstrating pneumococcal bacteremia, but not in less ill patients. Rapid administration of antibiotics is associated with improved survival. In the absence of known risk factors for Pseudomonas aeruginosa, dual antibiotic therapy (macrolide/fluoroquinolone + β-lactam) is usually recommended. However in the presence of Pseudomonas risk factors (long-term oral corticosteroids, frequent recent courses of antibiotics, severe structural lung disease [bronchiectasis, cystic fibrosis, very severe COPD]), anti-pseudomonal, an antipneumococcalβ-lactam/carbapenemplus ciprofloxacin/ levofloxacin is advised. Adherence to these recommendations has been associated with reduced lengths of hospitals stay and mortality. Many observational studies suggest a mortality benefit with atypical coverage especially with macrolides in severely ill patients. However, randomized controlled trials have not confirmed this benefit. Some but not all studies indicate steroids shortens the time to clinical stability. There may be a survival benefit in severely ill patientswith parenteral corticosteroids, but much larger randomized clinical trials are necessary to prove it. Significant numbers of patients will die even when appropriate antibiotics are administered in a timely fashion. These patients tend to have hypoalbuminemia and are non-ambulatory before hospital admission, suggesting that chronic underlying illness is driving outcome. This, unfortunately, implies that therapeutic interventions even when given appropriately and promptly, may not matter.

FUNGAL INFECTION IN RESPIRATORY FAILURE

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ABSTRACT

Respiratory failure is an inadequate gas exchange by respiratory system, which is a critical condition and require immediate treatment. Causes of respiratory failure are quite numerous and one of them is pulmonary fungal infection or mycoses. Endemic pathogense.g. *Histoplasma capsulatum, Cryptococcus neoformans, Coccidioides immitis, Blastomyces dermatitidis, Paracoccidioides brasiliensisand Sporothrix schenckii* are known as important cause of pulmonary mycoses. On the other hand,there are opportunistic fungi that cause infection in population with immune defect e.g. *Aspergillus, Mucor, Pneumocystis jiroveci* (causes PCP) and rarely by hyalohyphomycetes such as *Scedosporium, Fusarium and Paecilomyces*. Fungi enter human body by inhalation of the spore,then dependent on the immune status it can be eliminated or causes pulmonary infection. Fungal infections cause lung damage that can end up as respiratory failure.Critically ill patient often encourage doctors to be more focused on treating severe clinical symptoms and rule out diagnosis, which is actually very important. Awareness of clinician is the first step in the establishment of diagnosis, which then according to the clinical presentation the diagnostic steps is decided.Pulmonary mycosis is often found in Indonesia is invasive pulmonary aspergillosis-IPA, a common infection inpopulationwith hematological disorders and critically ill patients admitted to ICU. Furthermore, although rarely reported histoplasmosis, cryptococcosis, and mucormycosis can also cause a fatal pulmonary disorders. Diagnosis is combination of imaging, mycology investigations and biopsy. Imaging may provide a defined lung condition that is confirmed by mycological examination. For example, antigen test to detect galactomanan support the diagnosis of IPA.

Key words: respiratory failure, critically ill, aspergillosis, histoplasmosis,

INFLAMMATION BIOMARKER IN RESPIRATORY FAILURE

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ABSTRACT

Effective gas exchange in the lung requires thin alveolar septa with a minimum distance between the alveolar epithelium and the endothelium of the microvasculature to facilitate simple diffusion of those gases. When the endothelial-epithelial barrier is injured, interstitial and alveolar edema may develop, which, in turn, has a fundamental role in the development of acute respiratory distress syndrome (ARDS). Acute respiratory distress syndrome is a multifactorial syndrome with high morbidity and mortality rates characterized by a deficiency in gas exchange and lung mechanics, which leads to hypoxemia, dyspnea, and respiratory failure. The Berlin definition of ARDS emphasizes 3 ARDS categories—mild, moderate, and severe—based on the degree of hypoxemia.

The injury process in ARDS involves a complex interaction of numerous factors, including inflammatory cytokines, epithelial and endothelial damage, fibrogenesis, and abnormal lung mechanics.

Biomarkers of inflammation of ARDS consist of experimental biomarkers (IL-6, IL-8, TGF-β) and clinical biomarkers (TNF-□). Biomarkers of endothelial cell damage consist of experimental biomarker (VEGF) and clinical biomarker (Von-Willebrand factor, E-selectin and ICAM-1, Thrombomodulin, protein C and plasminogen activator inhibitor -1). Biomarkers of epithelial cell damage consist of experimental biomarker (PTEN deficiency) and clinical biomarkers (RAGE, KL-6, SP-D, CC16). Biomarkers of fibrogenesis consist of experimental biomarker (Versican, Decorin) and clinical biomarker (procollagen III, myofibroblasts and fibrocytes).

Regardless of improvements in the identification of biomarkers involved in ARDS pathogenesis, no single clinical or biologic marker reliably predicts clinical outcomes in ARDS. The combination of clinical and biologic markers may improve the sensitivity and/or the specificity of the test.

Although biomarkers are not now recommended for use in clinical practice with ARDS, biomarkers may be promising in developing and applying targeted therapies and in identifying candidates for clinical trials of novel therapies for ARDS.

NIV SETTING AND MONITORING
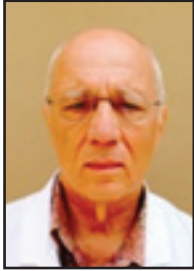
Nicolino Ambrosino
ITA

ABSTRACT

In acute exacerbations of COPD leading to acute respiratory failure, the work of breathing is increased due to increase in airway resistances. Due to lung hyperinflation the respiratory muscles are less effective and if the underlying pathology does not reverse in a relatively short time, they are at risk of failure and fatigue. Despite an increase in respiratory drive, rapid shallow breathing may lead to reduction in alveolar ventilation, even when minute ventilation is normal or even increased. Respiratory muscles progressively become unable to maintain adequate alveolar ventilation resulting in an increase of $PaCO_2$. When $PaCO_2$ is severely increased for prolonged time the level of consciousness is generally impaired.

When the cause of acute respiratory failure is reversible, medical treatment works to maximise lung function and reverse the precipitating cause, whereas the aim of ventilatory support is:
- To buy time in order the treatment of ARF cause does work;
- To decrease the work of breathing;
- To reverse the life threatening hypoxaemia and respiratory acidosis;

In these circumstances, inspiratory support works to increase alveolar ventilation by increasing tidal volume and to unload inspiratory muscles by decreasing the work of breathing. The addition of an external PEEP may further reduce it by counterbalancing the PEEPi.

The early use of NIV is mandatory because success rate decreases with disease progression. On the other hand, NIV may be useless or even be a trouble for the patient when applied in mild exacerbations which can be treated only by medical therapy. In practice arterial blood gases, and signs (tachypnoea or increased accessory muscle use) and symptoms (dyspnoea) of increased work of breathing should be used as markers to start NIV in these conditions. When NIV is started early, those patients not in danger (pH not lower than 7.30) can be managed outside the ICUs, eventually even in a ward with an adequately skilled team. In addition dedicated units like respiratory intensive care, high-dependency, should be promoted to deliver NIV to most but not all patients. For these patients, these units may offer noninvasive monitoring systems and higher nurse to patient ratios than in general wards with less burden but similar success rate than in ICUs.

Pressure pre-set modality of ventilation allows the patient to retain considerable control of breathing pattern and tidal volume. The usual advice, in COPD patients with increased $PaCO_2$, is to utilise pressure-limited ventilators as the first-line, especially in the pressure-assisted mode such as pressure support that delivers a pre-set Inspiratory Positive Airway Pressure to help every spontaneous breathing effort. With this modality, the patient's capacity to vary inspiratory time breath by breath is then warranted, and this allows a close matching with the patient's breathing pattern.

When setting the ventilator, the level of inspiratory pressure is progressively raised according to patient tolerance, with a minimum level of expiratory pressure around 4 cmH_2O in order to improve CO_2 removal by preventing rebreathingand counterbalance the PEEPi. During delivery of assisted-controlled NIV, a patient-initiated and adjustable trigger signal is able to synchronise the inspiratory phase, while a threshold

reduction of inspiratory flow is, most commonly, the cause for ventilator to cycle into expiration. It is possible, moreover, to select many other ventilator parameters such as "rise time" (time required to reach peak pressure), inspiratory time, inspiratory to expiratory ratio, backup respiratory rate in order to best match the patient's breathing pattern and characteristics. All these features may enhance the so called *"patient-ventilator synchrony"* and the overall comfort of NIV.

DIFFICULT TO WEAN IN INFANT TO CHILDREN
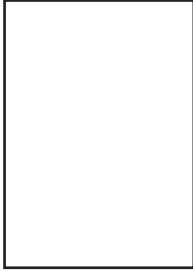
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ABSTRACT

Approximately 20 – 30% of ventilated patients are considered difficult to wean from mechanical ventilation devices due to multifactorial causes. To understand the patophysiology of weaning failure and develop a strategy to overcome it required a dedicated physician with an in-depth understanding.

Common practice in pediatric mechanical ventilation is based on personal experiences and this presents a barrier to planning and interpretation of clinical trials on the use of specific and targeted intervention. While The European Society for Pediatric and Neonatal Intensive Care initiated a consensus conference of international European experts in pediatric mechanical ventilation, the recommendation stated that there are insufficient data to recommend on initiation and approach to weaning and the use of any extubation readiness test (ERT) in not superior to clinical judgment.

In order to perform smooth weaning and successful extubation, several factors have to be addressed, i.e: factor impact weaning; predictive indices of weaning, techniques of weaning; weaning protocol; spontaneous breathing trial or extubation readiness test; and the use of adjunct support after extubation.

A structural framework ('ABCDE') for the assessment and treatment of difficult-to-wean patients would serve clinician better and earlier detection of the underlying problems. Thus, a tailored treatment strategy in order to reduce duration of mechanical ventilation can be design.

Keywords: difficult-to-wean; extubation readiness test; weaning failure

EARLY MOBILIZATION AND REHABILITATION PROGRAM IN INTUBATED PATIENTS

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ABSTRACT

Managing patient with mechanical ventilation is not only overcoming the complicated critical ill condition itself but also struiggling with the consequences of physical limitation resulted from the medical condition, prolonged immobilization and prolonged mechanical ventilation.

Critical ill polyneuromyopathy (CIPNM) affects weaning from mechanical ventilation and further impacts the outcome of functional capacity. The most important role in succeding weaning is diapragmn that is not uncommon affected in patient with mechanical ventilation, it is so called ventilator induced diaphragmn disfunction (VIDD).

Rehabilitation process for mechanically ventilated patient is not only treating the impacts of CIPNM and VIDD, buat more importantly is preventing rehabilitation to succed weaning process.

Early rehabilitation is initiated on respiratory muscles recruitment in breathing retraining, enhanching airway mucus clearance and initial basic activities. Furthermore, patient with mechanical ventilation is feasible and safe to out of bed mobulization in stable medically condition. It is closed supervisor and performed under team supervision.

Early rehabilitation and early mobilisation increase functional capacity for patient after mechanical ventilation.

Key words : *critical ill polyneuromyopathy, ventilator induced diaphragmn dysfunction, early rehabilitation, early mobilization.*

FIRST LINE ANTIBIOTIC IN SEPSIS

Sutji A Mariono

ABSTRACT

Sepsis is an infection with systemic manifestation of infection. Approach for sepsis including initial resuscitation, diagnosis, fluid therapy, vasopressor and antibiotic. Delay in administering antibiotic will result in increasing morbidity and mortality in sepsis patient. Thus, empirical antibiotic treatment is important and choosing the first line antibiotic become very crucial. History of patient's antibiotic therapy, pharmacodynamic and pharmacokinetic properties of an antibiotic and hospital microbial pattern are needed to be understood before choosing the therapy. The basic principal for empirical antibiotic treatment is early administration, broad spectrum antibiotic and prevent resistance. Empirical antibiotic treatment must be asses daily and de-escalation therapy to narrower spectrum must be done to reduce toxicity, to reduce cost and to prevent resistance. Culture of causative organism must be performed before administering the antibiotic and the result is important for de-escalation therapy. Clinicians then must decide whether to change or discontinue the antibiotic administration.

Keywords: Sepsis, antibiotic, de-escalation therapy

STRATEGIES TO OVERCOME INFLAMMATION IN ACUTE AND CHRONIC RESPIRATORY FAILURE

Dianiati Kusumo Sutoyo

ABSTRACT

Respiratory failure occurs when the respiratory system is unable to perform gas exchange function; oxygenation and/or carbon dioxide elimination. Respiratory failure may be found in acute or chronic condition. Inflammation plays a vital role in pathogenesis of respiratory failure. Acute respiratory distress syndrome (ARDS) is an example of acute respiratory failure condition where the inflammatory response which is triggered by direct or indirect insult will recruits neutrophils, activates macrophages, and produce several mediators. This condition will injure the lungs through increasing capillary permeability, microthrombus formation, and impaired hypoxic pulmonary vasoconstriction. In chronic respiratory failure such as in COPD patient, chronic exposure of cigarette smoke or irritants will cause persistent inflammatory process in the lungs. Both acute and chronic respiratory failure not only induce inflammatory response in respiratory system, but also lead systemic inflammation.

Regarding to the role of inflammation in respiratory failure, some pharmacological therapies might be the strategy to overcome inflammation process and its impact in respiratory failure. Corticosteroid is anti-inflammatory and immunomodulatorydrug that commonly used for patient with respiratory failure. Corticosteroid inhibits production of inflammatory cytokines such as tumor necrosis factor (TNF)-α, interleukin (IL)-1, IL-6, and IL-8. It also has a role to decrease collagen deposition that may cause fibrosis in both airway and lung parenchyma. Despite of its controversy, intravenous immunoglobulin (IVIg) also revealed potential effects of anti-inflammatory and immunomodulatory and might be the alternative treatment to treat respiratory failure beside corticosteroid. The mechanism of IVIg for those functions through modulation the expression of macrophage receptor, alteration of B and T cell, down-regulation of the inflammatory cytokines and chemokines, and interaction with autoantibodies.

Since pulmonary vascular resistance is increasing in respiratory failure, several vasodilator agents such as inhaled nitric oxide and prostacyclin may have beneficial effect to relax pulmonary vascular smooth muscle. Antioxidant is also believed giving better improvement in patient with respiratory failure. It overcomes the imbalance of oxidant and anti-oxidant that occurs during inflammation process

Since inflammation storm plays role and has detrimental effect, it will be the therapeutic target in respiratory failure patients. Although the results most of those agents are unsatisfied, it is still a promising target to help the improvement of patient with respiratory failure. Further researches are still needed for development of new drug therapy.

ABTRACT FREE PAPER

PRELIMINARY STUDY: THE PROFILE OF ELEVATED SOLUBLE UROKINASE PLASMINOGEN ACTIVATOR RECEPTORS LEVELS IN LUNG CANCER PATIENTS WHO RECEIVED CHEMOTHERAPY

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ABTRACT

Background: Lung cancer is a malignancy with the highest mortality rate in the world. Increased soluble Urokinase Plasminogen Activator Receptors (suPAR) levels positively correlated with stage, metastasis, and prognosis of lung cancer. Administration of chemotherapy may allegedly reducesuPAR levels. **Objective:** To analyze the profile of suPAR levels in lung cancer patients who received chemotherapy and its changes based on Response Evaluation Criteria in Solid Tumors (RECIST). **Methods:** suPAR levels were measured using ELISA in 18 lung cancer patients stage III or IV before (suPAR1), after third-cycle chemotherapy (suPAR2), and 9 patients after sixth-cycle chemotherapy (suPAR3). Data were presented in mean ± standard deviation. **Results:** Levels of suPAR1, suPAR2, and suPAR3 are 7.042 ± 3.116 ng/ml; 7.181 ± 3.641 ng/ml; 9.591 ± 5.895 ng/ml, respectively. suPAR2 levels in partial response (PR), stable disease(SD), and progressive disease (PD) are 9.509 ± 1.783 ng/ml; 3.552 ± 2.995 ng/ml; 6.782 ± 3.853 ng/ml, while suPAR3 levels in PR and PD are 12.073 ± 5.523 ng/ml; 4.626 ± 2.698 ng/ml, respectively. **Conclusion**: suPAR levels in lung cancer stage III and IV are in accordance with the spectrum of suPARlevels in malignancy. The levels of suPAR after chemotherapy did not show changes that corresponded to RECIST.

Key words: Lung cancer, chemotherapy, suPAR, RECIST

INTRODUCTION

Lung cancer is a malignancy with the highest mortality rate in the world where its incidence rate in Indonesia ranked first from 5 highest number of cancer cases among men and fourth among women in 2014. [1,2] suPAR is a new non-specific inflamation marker which role is to help the establishment of progression, prognosis and mortality of lung diseases and has the ability to liaise the molecular mechanism and the inflammation process.[3]The study conducted by Sumali in 2015 showed the decrease of uPA and uPAR levels in lung cancer patients after 4-6 cycles of chemotherapy with a significant difference in suPAR.[4]Further research is required to understand the spectrum of suPAR levels in lung cancer patients who receive chemotherapy so that it can be used as a reference in the monitoring and evaluation of chemotherapy success rate.

MATERIAL AND METHODS

This study has been accepted by the ethical committee and all the subjects involved have signed an informed consent. This study was conducted between December 2016 and December 2017 with an analytical descriptive design which was led in cohort towards 18 lung cancer patients who received treatment in Saiful Anwar Hospital (RSSA), Malang, Indonesia. The patients were followed up and their suPAR levels from serum were measured before (suPAR1) and after the third-cycle of chemotherapy (suPAR2), and 9 surviving patients were followed up until the sixth-cycle of chemotherapy (suPAR3).

The procedure of data retrieval and data collection is demonstrated in the flow chart showed in the figure 1 below.

Figure 1.Study flow chart.

The collected data is then analyzed by using the t-test and anova two way statistic evaluation. The statistic analysis used SPSS version 21. The average levels of suPAR will be presented in the form of mean + SD.

RESULT

This study includes 18 lung cancer patients who were followed since the pre-chemotherapy session until the third-cycle of chemotherapy, and among all patients, only 9 patients left who were followed up until the sixth-cycle of chemotherapy. The characteristics of all subjects are shown in the table 1 below.
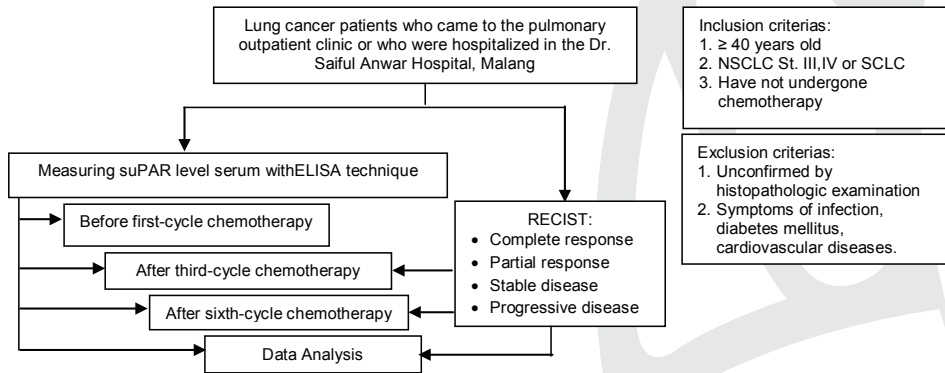
Table 1. Basic data characteristics of 18 lung cancer patients

Characteristics	Frequency(n)	Percentage(%)
1. Gender		
• Male	16	88.9
• Female	2	11.1
2. Age (year)		
• 40-49	3	16.7
• 50-59	5	27.8
• 60-69	6	33.3
• 70-79	2	11.1
• 80-89	2	11.1
3. Hereditary cancer (genetics)		
• Yes	2	11.1
• No	16	88.9
4. Education		
• Elementary School	3	16.7
• Middle School	5	27.7
• Secondary School	8	44.4
• University Diploma	1	5.6
• Undergraduate	1	5.6
5. Employment		
• Farmer	7	38.9
• Civil worker/Pensionary	3	16.7
• Furniture maker	1	5.6
• Cleaning service	1	5.6
• Paper factory employee	1	5.6
• Train railway mechanic	1	5.6
• Courier (expedition)	1	5.6
• Construction worker	1	5.6
• Bird breeder	1	5.6
• Housewife	1	5.6
6. Smoking History		
• Active smoker	13	72.2
• Passive smoker	5	27.8
• Non-smoker	0	0

Characteristics	Frequency(n)	Percentage(%)
7. Brinkman Index		
• Low (0-199)	2	15.38
• Medium (200-599)	6	46.15
• High (>600)	5	38.46
8. Type of Lung Cancer		
• NSCLC	15	83.3
• SCLC	3	16.7
9. Histopathology		
• *Non-small cell lung cancer (NSCLC)*		
- *Adenocarcinoma*	9	50.0
- *Squamous cell carcinoma*	5	27.2
- *Large cell carcinoma*	1	5.6
• *Small cell lung cancer (SCLC)*	3	16.1
10. Stage		
• Non-small cell lung cancer (NSCLC)		
- *IIIA*	3	16.7
- *IIIB*	2	11.1
- *IV*	10	55.5
• Small cell lung cancer (SCLC)		
- *IV (extensive stage)*	3	16.7

The patients who had received the third-cycle and the sixth-cycle chemotherapy were evaluated by examining the objective response based on RECIST as illustrated in the figure 2 below.
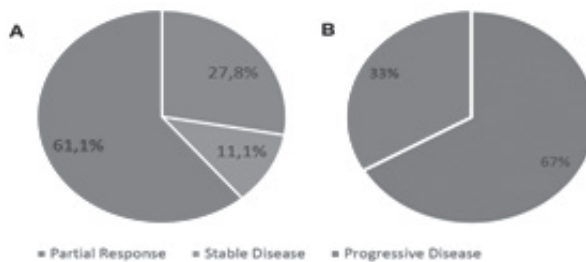
Figure2. Chemotherapy responses based on RECIST after the third-cycle (A) and the sixth-cycle (B) of chemotherapy.

The figure 3 below shows the suPAR levels (black dots) of the 18 lung cancer patients before the chemotherapy which are adjusted with the range of suPAR levels obtained from the literaturesthatinclude a healthy condition (0.1-4.0 ng/mL) in green, a low inflammation condition (> 4.0 – 10 ng/mL) in yellow, and a critical condition (> 10 ng/mL) in red.
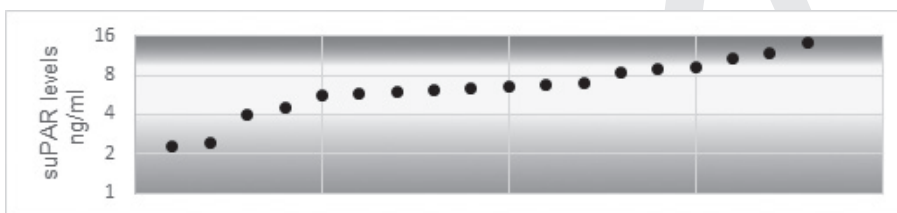
Figure 3. suPAR levels of lung cancer patients before chemotherapy.

The average of suPAR1, suPAR2, and suPAR3 levels are shown in the table 2 below.

Table 2. Spectrum of suPAR level before chemotherapy, after the third-cycle and the sixth-cycle of chemotherapy

suPAR Level (Mean ± SD)	suPAR1 (ng/ml) s (n = 18)	uPAR2 (ng/ml) (n = 18)	suPAR3 (ng/ml) (n = 9)
Lung cancer	7.042 ± 3.116 7	.181 ± 3.641 9	.591 ± 5.895

The values of suPAR1 and suPAR2 based on RECIST on the patients right after the third-cycle and the sixth-cycle of chemotherapy are summarized in the table 3 below.

Table 3. suPAR level based on RECIST on the lung cancer patients after the third-cycle and the sixth-cycle of chemotherapy

RECIST after chemotherapy	suPAR1 (ng/ml) Mean± SD	suPAR2 (ng/ml) Mean± SD	suPAR3 (ng/ml) Mean± SD
Third-cycle (n=18)			
Complete Response(n = 0)	-	-	
Partial Response(n = 5)	7.209 ± 3.610 9	.509 ± 1.783	
Stable Disease(n = 2)	5.181 ± 1.038 3	.552 ± 2.995	
Progressive Disease(n = 11)	7.305 ± 3.225 6	.782 ± 3.853	
Sixth-cycle (n=9)			
Complete Response(n = 0)	-	-	-
Partial Response(n = 6)	8.692 ± 3.893 8	.649 ± 2.349 1	2.073 ± 5.523
Stable Disease(n = 0)	-	-	-
Progressive Disease(n = 3)	8.492 ± 2.039 5	.439 ± 4.682 4	.626 ± 2.698

DISCUSSION
Subject Characteristics
In this study, the number of male (88.9%) is higher than female(11.1%).This fact is in accordance with the epidemiological data where the risk of lung cancer is approximately 4 times higher among men than women.[5]In 2014, WHO recorded the incident of lung cancer among men and women in Indonesia which attained 25,322 and 9,347 new cases, respectively.[1]

The highest number of lung cancer patients is among the age group between 60-69 years old(33.3%). This fact is in accordance with the literatures which states that after the age of 40 years, the risk of lung cancer increases progressively each year.[2]

There are 2 patients (11.1%) havehistory of hereditary cancer while 16 other patients (88.9%) do not have any history of hereditary cancer. Not all of lung cancer has a hereditary basis of cancer because in some

cases there are some type of cancers which may happen sporadically or without any history of family member who suffered from cancer. The cancer is not caused by a mutation in the germline or any genes which is susceptible to cancer, but it is more likely to be caused by the somatic genetic changes obtained.[5,6]

The highest number of the last education obtained by lung cancer patients is secondary school (44.4%). Education has a role as one of the factors which may increase the smoking activity among adolescent. This fact corresponds with the study about the determinant of smoking behavior among adolescent conducted by Alamsyah and Napianto: students who have lower level of knowledge constitute a risk factor of smoking behavior; students who do not attend any extracurricular activities at school have a higher risk of developing smoking behavior than those who attend it; and the majority of students have smoking behavior because they are exposed to the cigarette advertisement.[7]The data in this study is also in accordance with the Basic Health Research (Riskesdas) in 2013 which states that the highest number of daily smoker is found among the secondary school graduates, with the percentage of 28.7%.[8]

Most patients work as farmers (38.9%).Pesticides is commonly used to improve the quality and production of agricultural sector, which is a chemical substance, and thus generating negative influences, one of them is lung cancer.[9]Aside from the use of pesticides, the data obtained fromRiskesdas in 2013 indicated that farmers ranked first among regular daily smokers with the percentage of 44.5%, compared to those who are unemployed, employed or self-employed.[8]

There are 13 active smoker patients (72.2%) with the highest Brinkman index in the medium category (200-599 cigarettes/year) which included 6 smokers (46.15%) of them. As we know, smoking is one of the most essential risk factor that causes lung cancer. The cigarette smoke contains more than 300 chemical substances where 40 of theme are potent carcinogens, among them are NNK (Nicotine-derived Nitrosamine Ketone) and PAH (Poly-cyclic Aromatic Hydrocarbons) which can induce lung cancer.[5]

In this study, there are 5 patients (27.8%) who are passive smokers. The data obtained in this study is in accordance with theAmerican Cancer Societywho stated that 20% lung cancer patients in the USA have never been smoked previously.[10]Some of the lung cancer etiologies among non-smokers include age, environmental tobacco smoke or passive smokers, cooking fumes, diet, hereditary genetical vulnerability, exposure to carsinogen at the workplace or in the environment, hormonal factor, pre-existing lung disease and oncogenic viruses.[11]

In this study, the histopatologic overview of NSCLC patients consists of 9 adenocarcinoma patients(50%), 5 squamous cell carcinomapatients (27.2%), and 1 patient(5.6%) withlarge cell carcinoma, meanwhile the type SCLC consists of 3 patients (16.7%). Based on the literatures, adenokarsinoma, squamous cell carcinoma, andlarge cell carcinomaare included in the NSCLC category;whereadenocarsinomarepresents 40% andsquamous cell carcinomarepresents 20-30%; while SCLC category represents 15% of the whole lung cancer.[12]

In this study, either for NSCLC (55.5%)or SCLC (16.7%), the stage which has the highest number of patients is stage IV. Generally in Indonesia, lung cancer is diagnosed once the disease has already in the advanced stage, it is in accordance with the tumor profile in 2015 at RSSA where stage IV ranked first among the stages (92.7%).[13]

suPAR Levels and RECIST of Lung Cancer Patients

Based on the literatures, suPAR levels in a healthy condition ranges between 0.1 – 4.0 ng/mL, as for a low inflamation condition, the range of suPAR levels is between> 4.0 - 10 ng/mL which indicatesa 10-years increase risk of disease in cardiovascular, diabetes mellitus, cancerand mortality; while suPAR levels> 10 ng/mL indicates critical diseases such as sepsis, TB, HIV, and other acute infection with a high mortality risk.[14] In this study, suPAR1, suPAR2 and suPAR3 in the patients' blood serum were measured, resulting in the following levels: suPAR1 7.042 ± 3.116 ng/ml, suPAR2 7.181 ± 3.641 ng/ml, and suPAR3 9.591 ± 5.895 ng/ml.From the results above, it is revealed that there is an increasing trend of suPAR levels after chemotherapy. The suPAR levels in this study correspond with the previous studies conducted by Blasi & Sidenius, Eugen-Olsen et al., Noh et al., Gonias & Hu, Erkut et al.which states that suPAR levels increasedin some cases of cancer, where in this study, there are increased levels of suPAR in lung cancer patients. The levels of suPAR in lung cancer observed in this study are also corresponds with the levels of suPAR in cancer disease according to Eugen-Olsen which range between 4-10 ng/ml.[14]

The increase of suPAR levels after chemotherapy in this study has a difference with the study conducted by Linda in 2015, where there was a decrease of uPA and uPAR levels in the lung cancer patients after 4-6 cycles of chemotherapy with a significant difference in suPAR levels.4In accordance with Sumali, the suPAR levels obtained in the serum has shown a rapid decrease after a cytotoxic therapy for a patient with anacute myeloid leukemia (AML)in the study conducted by Erkut.[15]

In his study, Mustjoki et al.has found that a high level of suPAR in the plasma is related with the resistance towards chemotherapy in the case of AML.16 Apart from the resistance towards chemotherapy, the efficacy of chemotherapy may decline in front of the cells which contain uPAR because the existence of this type of cells indicates a cancer stem cell, which are CD44 and MDR1. CD44 is a cell membran bound glycoprotein expressed in various types of tumor cells and is a significant factor in the growth of tumor, invasion and metastasis. In SCLC, the activation is obtained from the CD44-MAPK-PI3K signal resulting in the increase of uPA, uPAR and MDR1 expression which cause the tumor cells to be more invasive and become resistant towards any cancer medication. The chemotherapy agents target the majority of cancer cells, while the rest of the lung cancer stem cells can regenerate the cancer cells population so that it can produce a tumor relapse right after the chemotherapy.[17]

On one hand, the uPAR expression can also increase the cellular viability by stimulating the anti-apoptotic pathways.18The uPA-uPAR interaction may encourage the cellular viability by activating the Bcl-2 and Bcl-xL anti-apoptotic transcription factor through the MEK/ERK and PI3K/Akt pathway, where those mediators become the base anti-apoptotic activities through the uPA-uPAR interaction.[19]

On the other hand, in the case of solid cancer in vivo, which is the lung cancer for this study, it is still debatable whether if the raise of suPAR levels in cancer patients' plasma is originated only from the tumor cells or from the macrophages infiltration in tumor; because in solid cancer, apart from being expressed by the cancer cells, uPAR is also expressed by the stromal cells.[16]

The ELISA techniques could not be used to differentiate whether if the produced suPAR cell is an expression of the epithelial cancer cell or also comes from the stromal. Besides, in the ELISA examination, the complexes which are not present in the tissue can also be generated because various components and cells in tumor can be carried away in the extract. Due to the high number of antigens which heterogeneously distributed

in the tumor, including the component of plasminogen activation system, the buffer extraction during ELISA procedure should be taken into account.[20]

The RECIST used in this study corresponds with The Indonesia Society of Respirology, as follows : 1. Complete response (CR) if during the evaluation, the tumor is 100% disappeared and that this condition remains for more than 4 weeks; 2. Partial response (PR) if there is a reduction of the tumor size as many as >50% but <100%; 3. Stable disease (SD) if the tumor size does not change at all or or there is a reduction as many as >25% but <50%; and 4. Progressive disease (PD) if there is anincreasing of tumor size for >25% or a new tumor/lession has appeared in the lung or in another place.[21]

There are 18 patients who had undergone the third-cycle of chemotherapy with the RECIST-based chemotherapy response evaluation as follows: 5 PR patients (27.8%), 2 SD patients (11.1%), and 11 PD patients (61.1%). From all 18 patients who have been followed, there are 9 deceased patients after the third-cycle of chemotherapy with the following RECIST: 1 PR, 2 SD and 6 PD. Hence, there were only 9 patients left who could be followed and who have finished the chemotherapy session successfully up until the sixth-cycle with RECIST (compared to the torax CT scan right before the chemotherapy): 6 PR patients (66.7%) and 3 PD patients (33.3%).

In this study, none of the patient has reached the RECIST-based complete response, because all patients were already in the advanced stage since the beginning (the majority of them were in the stage IV), where the objective of chemotherapy session during the advanced stage is no longer curative but paliative.[22]

According to the t-test result, it is demonstrated that there is no significant difference between the RECIST-based suPAR levels in the patients either before and after the third-cycle of chemotherapy, or before and after the sixth-cycle of chemotherapy ($p > 0.05$). This result is not in accordance with the hypothesis of our study which indicated that after the chemotherapy session, the suPAR levels in the lung cancer patients are reduced with a positive response compared to those with a negative response. In contrast with the study conducted by Dohn et al., he obtained a significant relation between the positive value of uPAR and the T stage found in the cancer cells, macrophages and miofibroblast in the tumor core.[23]

There are some causative factors generating the inexistence of significant difference between suPAR levels based on RECIST. Currently, the chemotherapy responses are measured radiologically, commonly using CT scan or MRI. The response criteria for the solid tumor which has undergone a therapy with the cytotoxic agents is the RECIST criteria, which is based on the evolution of tumor size. The RECIST criteria becomes inappropriate in certain circumstances such as when the cancer has already spread up until the pleura.[24]

Besides, generally the lung cancer patients receive treatment during the advanced stage, corresponding to this study, none of the patients has reached the complete response, and the suPAR level which did not show any sign of reduction, either after the third-cycle or the sixth-cycle of chemotherapy. The aim of chemotherapy during the advanced stage of cancer is no longer as a curative therapy but as a paliative one, which is to reduce or to eliminate the symptoms caused by the growth of cancer cells in order to improve the quality of the lung cancer patients' life.[14]

Offers net al. states that urokinase Plasminogen Activator (uPA) and Plasminogen Activator Inhibitor-1 (PAI-1) are not related to the clinical or the pathological parameter (histopathology type), stage (T and N

classification) and age, as well as the overall life expectancy of the patient. The components of plasminogen activation system only constitute some of the factors which play a role during the tumor development, so that it is safe to conclude that there are a lot more factors in the tumor development.[15, 25]

In this study, there are increased levels ofsuPARin stage III and IV lung cancer patients after the third-cycle and the sixth-cycle of chemotherapy, compared to the levels before chemotherapy.The levels of suPAR after chemotherapy did not show changes that corresponded to RECIST.

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SSOCIATION OF INTERLEUKIN 17F rs763780 GENE POLYMORPHISM ON THE SUSCEPTIBILITY TO DRUG SENSITIVE PULMONARY TUBERCULOSIS AND DRUG RESISTANCE PULMONARY TUBERCULOSIS IN MALANG INDONESIA

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BACKGROUND

Tuberculosis (TB) is a world major health problem. In 2014, it is estimated that there were 9,6 million new TB cases. The death rate of TB around the world is 1,5 million people, 1,1 million of is HIV-negative, and 0,4 million is HIV-positive. Indonesia is one of three country with the most TB cases, aside from India and China with total case number of 10% from total world TB cases1. TB prevalence in Indonesia is 0,4% from total population, most of the cases occur in age group 25 – 34 years in the amount of 20,76% and cases in men is 1.5 times greater than women[2].

It is not clear why someone infected by Mycobacterium tuberculosis (Mtb) can become sick while the other only showed effective immunity system which can survive this infection. From all people infected Mtb only 5 – 10% developed active tuberculosis[3]. Study in monozygot twin indicated that genetic factor plays a role in infection suspectibility[4]. It is predicted that initial immunity respone in Mtb infection will determine the course of disease. In suspectible people, body immunity failure to eliminate Mtb caused the rise of Mtb population which become a risk for mutation, this can lead to drug resistant TB[5].

T helper 17 lymphocyte cell (Th 17 cell) is a new subset of T lymphocyte. This cell act as a main cell which produce Interleukin 17 (IL-17). In tubeculosis infection, IL-17 act as an initial inflamation mediator, forming of mononuclear granuloma, and neutrophile recruitment. IL-17 deficiency caused suboptimal granuloma formation, which leads to the rise of Mtb population and become a risk factor for dissemination. Beside that, interleukin 17 supports Th1 cell function to optimalize control of tuberculosis infection[6].

A fair amount of studies in interleukin 17 polymorphism and suspectibility of TB have been conducted across the world but the results still inconsistent. Study in China mentioned IL-17F rs763780 polymorphism linked with tuberculosis suspectibility[7]. But study in Croatia said that IL-17A and IL-17F polymorphism weren't associated with tuberculosis suspectibility[8]. A rather interesting thing found in Brazil study, which reported that IL-17A polymorphism associated with lower risk of tuberculosis instead[9]. Metaanalysis result showed that IL-17F rs763780 linked to tuberculosis suspecibility in Asian but this study has limitation with small sample size. Until recently, no study has been conducted for IL-17F rs763780 polymorphism in lung tuberculosis, including drug resistant lung tuberculosis in Indonesia. This study aimed to know whether IL-17F rs763780 gene polymorphism caused suspectibility in drug sensitive and drug resistant lung tuberculosis in Malang, Indonesia

METHOD
Population Study

This study used case control design to find out IL-17F rs763780 polymorphism in drug sensitive lung tuberculosis (DS TB) and drug resistant lung tuberculosis (DR TB). Sample size was 80 people, consist of 27 DS TB patient, 27 DR TB patient, and 26 healthy subjects. All ethnic treated in lung outpatient or inpatient clinic at dr. Saiful Anwar Malang Hospital were included in the study and recorded. DS TB and DR TB diagnosis is based on sputum examination with Xpert/Mtb/Rif method and chest X-ray. The control group is healthy subject. In this group, chest X-Ray was taken first to exclude the possibility of active lung TB

infection. Inclusion criteria were: patient diagnosed with drug sensitve lung tuberculosis, drug resistant lung tuberculosis, age 14 – 65 years old, agree to participate in this study and sign informed consent. Exclusion criteria were: HIV-AIDS patient, patient who has chronic kidney disease, diabetes mellitus, autoimmune disorder, or pregnant. We used questionaire to collect TB patient and control group demographic data, which were age, sex, smoking or not smoking, education, and income. All subject gave permission and signed writen informed consent before joining the study. Our study protocol had been approved by Saiful Anwar General Hospital ethical committee.

Genotype Analysis

RFLP (Restriction Fragmen Length Polymorphism) was used for genotype analysis in this study. Vein blood was taken with 3 cc needle aspiration and contained in EDTA tube then stored in -200 C frezeer until it was analyzed. Salting out method based on manual protocol was used for DNA extraction. PCR process began with mixing 90 μL Go Taq Green PCR mix, 45 μL H20 free nuclease and 5 μL primary each forward 5 - GTT CCC ATC CAG CAA GAG AC - 3 and reverse 5 – AGC TGG GAA TGC AAA CAA AC – 3, then each of them was taken as much as 5 μL and mixed with 1 μL DNA which had been isolated and put into the PCR machine (BIO RAD C1000 Thermal Cycler) with initial denaturation protocol at 940C for 45 seconds, annealing 620C for 60 seconds, extension 720C for 60 seconds. Final extension was done in 720C for 10 minutes10. Tracking alele where the polimorphism occured was done by incubating PCR product with NlaIIIrestriction enzym (New England Biolabs Ipswich, MA. USA). PCR result was electrophored in 2.5% agarose gel and visualized with UV light and ethidium bromide coloring. The product of this RFLP method were CC, TT, and CC genotype. CC genotype was shown by 410bp and 291bp product , CT 410bp, 291bp and119bp product, TT 291bp and 119bp product.

Statistical Analysis

Data complation and analysis was done by using IBM SPSS version 20.0 software. Continous variables are shown as mean ± standard deviation (SD), and categorical variables are shown as frequency and percentage (%). Chi square or x^2 test was used for comparing continous and categorical variable between case and control group. Relation between polymorphism and lung tuberculosis was analyse by chi square test with confidence interval 95%, **α**=0,05, significant if $p<0.05$. Whereas, odds ratio (OR) was conducted to determine how strong is the risk factor

RESULT

Sociodemographic Features

Average age in DS TB case group was 35.37 years, in DR TB group was 37.15 years, and in control group was 27.19 years. Mann Whitney test shown that control group age average was significantly different compared with DR TB and DS TB group. There was a significant difference in income level between case and control group. There was no significant difference between sex, marital status, smoking status, eduction, and occupation (Table 1).

Table 1. Sociodemographic Features

Features	Control		Case				Total		P
	N = 26		DS TB N = 27		DR TB N = 27		N=80		
	n	%	n	%	n	%	n	%	

		n	%	n	%	n	%	n	%	P
Age	Minimum		18		18		22		18	0.014[a]
	Maksimum		37		58		65		65	
	Rata-rata±SD		27.19±6.09		35.37±13.2		37.15±12.6		33.31±11.8	
Sex	Man	15	57.69	14	51.85	18	66.67	47	58.7	0.268
	Women	11	42.31	13	48.15	9	33.33	33	41.2	
Mariage	Yes	16	61.54	18	66.67	23	85.19	57	71.3	0.111
	No	10	38.46	9	33.33	4	14.81	23	28.7	
Smoking	Yes	3	11.54	14	51.85	17	62.96	34	42.5	0.477
	No	23	88.46	13	48.15	10	37.03	46	57.5	
Education	S1	25	96.15	9	33.33	12	44.44	46	57.5	0.409
	D3	0	0.00	1	3.70	1	3.70	2	2.5	
	High School	1	3.85	17	62.96	10	37.04	28	35	
	Junior School	0	0.00	0	0.00	4	14.81	4	5	
Occupation	Seller	0	0.00	2	7.41	4	14.81	6	7.5	0.260
	Swasta	3	13.04	15	55.56	18	66.67	36	45	
	House wife	0	0.00	4	14.81	3	11.11	7	8.75	
	Farmer	0	0.00	2	7.41	2	7.41	4	5	
	Student	23	88.46	3	11.11	0	0.00	26	32.5	
	Retiree	0	0.00	1	3.70	0	0.00	1	1.25	
Income	> 3.5 Jt/bulan	0	0.00	4	14.81	2	7.40	6	11.1	0.033[b]
	2.5-3.5 jt/bulan	2	7.69	6	22.22	8	29.62	16	29.6	
	1.5-2.5 jt/bulan	0	0.00	9	33.33	11	40.74	18	33.3	
	< 1.5 jt/bulan	0	0.00	8	29.62	6	22.22	14	25.9	

a:ujiKruskal Wallis, b:ujichi square, SD: Standard Deviation, DRTB: Drug Resistant Tuberculosis, DS TB: Drug Sensitive Tuberculosis

Clinical Feature

The main symptom in DS TB group was prolonged cough, as much as 55.55%, whereas the most frequent main symptom in DR TB is shortness of breath, up to 62.96%. The most common chest X-Ray result in both case groups was far advance lesion, but this feature is more common in DR TB group, 77.78%(Table 2). The most prevalent type of drug resistant TB patient was relapse case, 12 people (44.4%), while the least was new case, 2 people (7.4%) (Figure 2).

Table 2. Clinical Feature

Variable D		S TB D		R TB T		otal P		
	n	%	n	%	n	%		
Chief Complaint								
Dyspnoe	7	25.92	17 6	2.96 2	4	44 0		.007
Chronic cough 1	5	55.55	2	7.40 1	7	31		
Chest pain 1	3	.70	1	3.70 2	4			
Hemoptysis 3	1	1.11 6	2	2.22 9	1	7		
Decreased of body weight 1	3	.70	1	3.70 2	4			

Chest X Ray							
Far advanced lesion	15 5	5.55 2	1	77.78	26 6	7	0.024
Milier 2	7	.40	0	0.00 2	4		
Moderate lesion	4	14.81	6	22.22	10 1	8	
Minimal lesion	6	22.22	0	0.00 6	1	1	
Xpert/MtbRif Sputum							
Very low	3	11.11	2	7.40	5	9	0.943
Low	8	29.62	7	25.92	15 2	9	
Medium	8	29.62	9	33.33	17 3	1	
High	8	29.62	9	33.33	17 3	1	
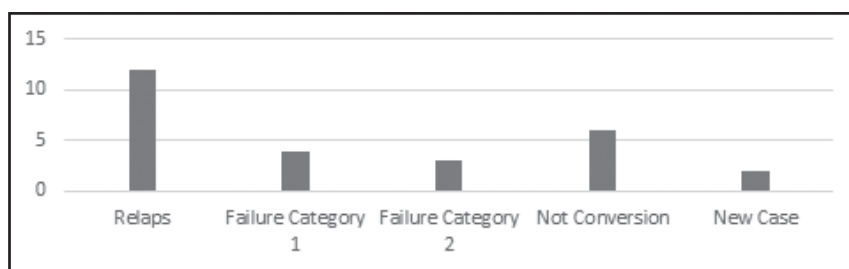
Figure 2. Distribution of DR TB patients

Distribution of Alele and Genotype

Alele T and TT genotype TT were most commonly found in healthy control group (65.4% and 80.8% respectively). Alele C was most frequently found in DR TB and DS TB. In DS TB, C alele is most commonly found in CT genotipe group (heterozygote), whereas C alele distribution in DR group was in CC genotipe group (homozygote). There was no significant difference in C alele and CT genotipe distribution between DR TB and DS TB group compared to control group(Table 3).

Table 3. Distribution ofAlele and Genotype IL-17F rs763780

Variable D	S TB D		R TB C		ontrol		P	P* P	**
	N	%	N	%	N	%			
TT 4	1	4.8	6	22.2 1	7	65.4 0	.002 0	.012 0	.431
CT 1	4	51.9 9	3	3.3	8	30.8 0	.068 0	.744 0	.137
CC 9	3	3.3	12 4	4.4	1	3.8	0.000	0.000	0.432
Alele T	22 4	0.7	21 3	8.9 4	2	80.8 0	.001 0	.001 0	.842
Alele C	32 5	9.3 3	3	61.1 1	0	19.2 0	.147 0	.225 0	.878

P: DR TB vs control; P*: DR TB vs control; P**: DS TB vs DR TB

Statistical Analytic ofPolymorphism Examination

CC and CT genotype prevalence in DS TB group was greater than the control group (Table 4). There was a significant relationship between CC and CT genotype with the risk of DS TB (OR 8.09; 95% CI= 1.24 –

52.57 and OR 2.44; 95% CI= 1.35 – 4.40). In overall, individuals with C allele increase susceptibility to drug sensitive tuberculosis.

Table 4.Association of Polymorphismin DS TB group vsControl

Variable D		S TB C		ontrol O		R (95%CI)	P
		N	%	N	%		
Genotype T	T	4	14.8	17 6	5.4	ref	
C	T	14 5	1.9	8	30.8	2.44 (1.35 – 4.40)	0.001
	CC 9	3	3.3	1	3.8	8.09 (1.24 – 52.57)	0.000
Alele T		22 4	0.7	42 8	0.8	ref	
Alele C		32 5	9.3	10 1	9.2	15.1 (3.55 – 64.21)	0.000

DS TB: Drug Sensitive Tuberculosis

Prevalence of CC and CT genotype in DR TB group was greater than the control group (Table 5). There was a significant relationship between CC genotype with the risk of DR TB (OR 9.45; 95% CI= 1.41 – 63.23). there was no significant relationship between CT genotype and the risk of DR TB (OR 1.57; 95% CI= 0.89 – 2.74). In overall, individuals with C allele also increase susceptibility to drug resistant tuberculosis.

Tabel 5.Association of Polymorphismin DR TB group vsControl

Variable D		R TB C		ontrol O		R (95%CI)	P
		N	%	N	%		
Genotype T	T	6	22.2 1	7	65.4 r	ef	
C	T	9	33.3 8	3	0.8	1.57 (0.89 – 2.74)	0.083
	CC 1	2	44.4 1	3	.8 9	.45 (1.41 – 63.23)	0.000
Alele T		21 3	8.9	42 8	0.8	ref	
Alele C		33 6	1.1 1	0	19.2	6.61 (1.96 – 22.27) 0	.002

DR TB: Drug Resistant Tuberculosis

DISCUSSION
Sociodemographic Features
There was no significant sociodemographic feature in DR TB and DS TB average age, but there was a significant difference compared to the control group (p=0.014). Average age in DR TB and DS TB group can be categorized in productive adult age. This is in accordance with WHO report in 2015 and Ministerial of Health Regulation in 2016 which stated that the most prevalent tuberculosis incident is found at productive adult age group. Adult tuberculosis incident is 1.5 – 6 times more that children and adolescent age group. This is happened because there is greater contact in household and neighborhood in adult group, especially in adult men[11].

Subject's income in DR TB and DS TB group is most commonly in the range of 1.5 – 2.5 millions rupiah per month (moderate income). A 2012 study in India found that the highest prevalence of tuberculosis was found in poor community. Poverty is associated with lack of nutrition, inadequate access to health services and poor enviroment sanitation. All factors mentioned above are associated with the risk of tuberculosis transmission and disease[13].

Clinical Features

There was difference in main symptom between DS TB and DR TB group (p = 0.007). DS TB group was mostly complained about prolonged cough for more than 2 weeks where as DR TB group complained were shortness of breath. According to studies in Ethiopia and India, the most common symptom found in lung tuberculosis patient is prolonged cough for more than 2 weeks[14,15]. Other studies also stated that there was no significant difference in clinical manifestation between DS TB and DR TB unless it is concomitant with HIV infection[16,17]. In this study, most of the DR TB subject had been infected with tuberculosis before so the main symptom was more severe. This in in accordance with study in Brazil which mentioned that outcome in MDR TB is worse than DS TB[18].

X-ray findings in DS TB and DR TB group was widespread lesion (far advanced lesion). This is in line with study in Vietnam which said that widespread lesion, including cavity, consolidation, and fibrosis were the most common lesion found, particulary in men[12]. Other study further proved a more extensive damage in DR TB group, which include cavity, consolidation, bronchiectasis, atelectasis, bullae, and calsification[19].

Alele Frequencies and GenotipeIL-17F rs 763780

In healthy control group, T alele and genotipe TT were more frequent that alel C. This is in accordance with studies in China and Croatia[7,8,20]. T alele and TT genotype are alele that commonly found in healthy control group at Caucasian and Asian population so that can be expected that these T alele and TT genotype give protective effect to lung tuberculosis in most races, including Malayan Mongoloid tribe[20]. It turns out that protective effect of TT genotype in lung tuberculosis is not evident in other disease. A study in Japan mentioned that TT genotype is a risk factor of ulcerative colitis whereas C alele gives protective effect in that disease[21]. This findings are supported the consept of variability of genetic suspectibility to different diseases[20].

We found that alele C, CC and CT genotype prevalence was higher in lung tuberculosis group (both drug sensitive and drug resistant) compared to the control group. That similiar result is obtained if the comparasion was done between DS TB and DR TB group with healthy control. This result is similiar with a study in China[7,20]. Interestingly, in this study we found a much higher prevalence compared to the study in China. CC and CT genotype prevalence in our study was 38.8% and 42.6%, whereas at the study in China it was 1.7% and 25.3% and also 9.23% and 16.01%. A 2015 study in Croatia (Caucasian) which also count the prevalence of CC and CT genotype prevalence and found a lower CT genotype prevalence, 5.36%, and didn't find any CC genotype. This difference is accounted to racial difference between Asian and Caucasian[22]. We found genotype CC prevalence (homozygote) was higher in DR TB compared to DS TB. Until now, there is no other study which count CC genotype prevalence in DR TB group so our study can become a reference for other study in the same topic. We also found 8 people (30.8%) with CT genotype polymorphism and 1 person (3.8%) with CC genotype polymorphism in healthy control group. This result is in line with study in China which also found this genotype polymorphism in healthy control group with smaller prevalence than case group[7].

Relation Between IL-17F rs 763780 Polymorphism and Lung Tuberculosis Suspectibility

Our result found there was a significant relationship between IL – 17F rs 763780 polymorphism to suspectibility for lung tuberculosis in DS TB or DR TB group with CC genotype (OR 8.09; 95% CI= 1.24 – 52.57; OR 9.45; 95% CI= 1.41 – 63.23). There was also a significant relationship in CT genotype (OR 2.44; 95% CI= 1.35 – 4.40) in DS TB group only. This findings are consistent with study in China but contradictive with study in India and Croatia which stated there was no relationship between IL – 17F rs

763780 polymorphism and suspectibility to tuberculosis[7,8,20,23,24]. Meta-analysis study found there was a significant relationship in C alele and CT gentoype only in Asian. This difference is accounted to ethnical difference between Asian and Caucasianand supports the theory that genetic factor may have an effect in tuberculosis infection. Besides that, this difference is also associated with difference in economic status between Asian and Caucasian[22].

IL-17F rs763780 polymorphism causes decline in IL-17F quality. IL-17F polymorphism in the 3rd exon causes substitution in His (Histidine) amino acid to Arg (Arginine) which causes disorder in intracelular signalling that causes IL-17 loses it's ability to induce proinflamatory protein synthesis[25]. IL-17 function disorder in tuberculosis causes disorder in mononuclear granuloma formation, neutrophil and other inflammatory cells recruitment which facilitate spread of Mtb infection[6]. It is unclear whether IL-17F rs763780 polymorphism also affect IL-17F level in lung tuberculosis patient. Abimanyu et al found that there was no significant relation between IL-17F polymorphism and it's level in blood between tuberculosis patient and healthy subject[24].

Interestingly, our study found a higher suspectibility in individuals with CC genotype (homozygote) both in DS TB and DR TB group. Until now there are few study which associated genotype difference with IL-17F level or it's cytokine production quality. Abhimanyu et al found that there was no significant difference in IL-17F level between TT and CT genotype between lung tuberculosis group and control group[24]. In asthmatic patient, both IL-17A and IL-17F level increased compared to healthy subject but there was a significant difference in IL-17F level between TT and CT genotype, in which IL-17F plasma level was almost 10 times lower in CT genotype compared with TT genotype[26]. T alele is dominant and C alele is minor alele. Because of that we predict that individual with CC genotype (homozygote) has lower IL-17F level than CT genotype individual (heterozygote). This lower level hinders IL-17F/IFN-ɣ axis which in turn increase the suspectibility to tuberculosis[6].

CONCLUSION
1. C alele, CT genotype, and CC genotype prevalence in drug sensitive lung tuberculosis and drug resistant lung tuberculosis was higher than healthy control group

2. IL-17F rs763780 polymorphism caused suspectibility to drug sensitive lung tuberculosis (OR 15.1; 95% CI = 3.55 – 64.21)

3. IL-17F rs763780 polymorphism caused suspectibility to drug resistant lung tuberculosis (OR 6.61; 95% CI = 1.96 – 22.27)..

4. In drug sensitive tuberculosis group, individual with CC genotype (homozygote) IL-17F rs 763780 polymorphism had 3 times more risk compared to CT genotype (heterozygote), whereas in drug resistant tuberculosis group the risk of CC genotype was 6 times higher compared with CT genotype

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THE EFFECT OF OPHIOCEPHALUS STRIATUS EXTRACT ON IL-17 AND suPAR LEVELS, LUNG DIFFUSIN CAPACITY (DLCO), AND QUALITY OF LIFE IN STABLE COPD PATIENTS WITH MUSCLE WASTING

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ABTRACT

Background : Muscle wasting is an extrapulmonary manifestation found in 50% COPD patients that causes a decrease in quality of life (QoL). The complexity of inflammatory cytokine involved in COPD plays a role in the occurance of skeletal and respiratory muscle wasting, which further affects the DLCO. The aim of this study is to establish the effect of *Ophiocephalus striatus* extract – oral nutritional supplement enriched in protein and amino acids – in reducing the levels of IL-17 and suPAR, and also to improve the DLCO and the QoL of COPD patients with muscle wasting.

Methods : This was a clinical study with quasi experimental method, which involved 32 COPD patients with muscle wasting at Pulmonology Outpatient Clinic of Saiful Anwar General Hospital Malang. They were given *Ophiocephalus striatus* extract for 12 weeks. The measurement of serum inflammatory cytokine level, DLCO, and QoL were performed before and after nutritional intervention.

Result : A non-significant reduction of IL-17 and suPAR occured after 12 weeks (p=0.275 and 0.67, respectively). The DLCO improved insignificantly as well (p=0.369). However, the QoL increased significantly as assessed by CAT score (p=0.000). There was no significant correlation between the level of those inflammatory cytokines and DLCO nor the CAT score.

Conclusion : Ophiocephalus striatus extract was successful in decreasing IL-17 and suPAR level, also in improving DLCO. Moreover, the QoL improved significantly after nutritional supplementation. The present study results suggest a potential role for the administration of oral nutritional supplementation in the management of COPD patients with muscle wasting.

Keywords : *Ophiocephalus striatus* extract, COPD, muscle wasting, IL-17, suPAR, DLCO, CAT

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a preventable and treatable disease, which is characterized by persistent airflow limitation that is usually progressive and associated with chronic inflammatory response in the airway to noxious particles or gases.[1] Muscle wasting is one of the extrapulmonary manifestation which occurs in 50% of COPD patients. It caused by the imbalance of protein synthesis and degradation, which is a consequence of systemic inflammatory response occuring in COPD.[2,3,4]

IL-17 and suPAR are known as fibrogenic cytokines, which will activate fibroblast and trigger fibrosis in the lung and airway. IL-17 induced lymphoid tissue leading to an influx of neutrophils and macrophages into the airways followed by the production of elastase, a potent enzyme causes hyperresponsiveness airway and tissue remodeling.[5,6] Meanwhile suPAR induced matrix metalloproteinase deposition resulting in fibrosis in several tissues including lung and muscle.[7]Systemically, they cause increased collagen production, impaired muscle cell regeneration, and diaphragm weakness. Severe fibrosis occurs in various tissue causes systemic effect like cachexia and muscle atrophy.[8]

Patients with reduced muscle mass tend to experience more severe gas trapping, lower diffusing capacity, and more limitation in activity than patients with the same respiratory condition but with normal body weight. The loss of body cell mass associated with decreased diaphragm mass and respiratory muscle, resulting in decline of respiratory system strength and endurance.[9,10]

Additional nutritional supplementation promotes significant gain in fat free mass among COPD patients especially if malnourished. In addition, it increases respiratory muscle strength and exercise capacity resulting in better quality of life.[1] Ophiocephalus striatus extract enriched in albumin, protein, amino acids, and polyunsaturated fatty acids is one of oral nutritional supplementation that can be considered for patients with chronic diseases, including COPD.

The aim of this study is to determine the effect of *Ophiocephalus striatus* extract in IL-17 and suPAR levels, diffused lung capacity for carbonmonoxide (DLCO), and the quality of life of COPD patients with muscle wasting, so it can be considered as a nutritional therapy which is a part of holistic therapy for COPD comorbidities.

METHODS
This is a clinical research using pre and post intervention quasi experimental conducted at Pulmonology Outpatient Department Dr. Saiful Anwar General Hospital Malang since January until June 2017. Consecutive sampling is done in this study, which means every patient who meets the study criteria and is willing to participate in the research is taken as the sample until fulfill the number of samples. The minimum sample size in this study is 28 people.

The inclusion criteria were males, age between 40-65 years old, diagnosed with stable COPD and received standard therapy according to GOLD 2015, have muscle wasting comorbidity, willling to participate in this research and sign the informed consent letter. The exclusion criteria were COPD patients with muscle wasting but have other systemic comorbidities such as diabetes mellitus, chronic heart failure, malignancy, cerebrovascullar disease

Patients who met the inclusion and exclusion criteria performed physical examination and Body-electrical Impedance Analysis (BIA) to determine Body Mass Index (BMI) and Fat Free Mass (FFM). Study subjects filled out the COPD Assessment Test (CAT) questionnaire as QoL parameter, then IL-17 and suPAR levels were examined by ELISA technique with venous blood sample, and diffused lung capacity were examined by body plethysmography. The intervention given was administration of *Ophiocephalus striatus* extract – an oral nutritional supplementation – 500 mg three times daily for 12 weeks. After supplementation, the same examination as before were done.

Data collected was processed and analyzed using IBM SPSS statistics series 23.0. The statistical test used as comparative test is paired T test and Wilcoxon, while correlative test using Spearman and Pearson correlation test.

RESULT
There were 33 patients who meet the inclusion and exclusion criteria. During the research, 1 patient was passed away before the end of this study. Characteristic of the study subject was shown in Table 1. All of the study subjects were male with the mean age was 62,72 years old. Most of the subjects was above 60

years old (25 patients ; 78,13%). All of the study subjects were ex smoker with various degree of severity based on Brinkmann Index and the majority was heavy smoker. According to COPD population, 18 subjects (56,25%) was in group D population, which is the more symptoms and high risk group. 50% of subject's Body Mass Index (BMI) was in normoweight group, but according to Fat Free Mass all of the subjects have muscle wasting condition.

Table 1. Subject Characteristics

Characteristics	Frequency	Percentage (%)
Age (years)		
∞45-50	1	3,13
∞51-60	6	18,75
∞> 60	25	78,13
Sex		
∞Male	32	100
∞Female	0	0
Brinkmann Indeks		
∞Mild (0-199)	4	12,5
∞Moderate (200-599)	13	40,63
∞Heavy (> 600)	15	46,87
COPD population		
∞Group A	3	9,38
∞Group B	9	28,13
∞Group C	2	6,25
∞Group D	18	56,25
Body Mass Indeks (BMI)		
∞Underweight (< 18,5)	13	40,63
∞Normoweight (18,5-24,9)	16	50,00
∞Overweight (> 25)	3	9,38
Fat Free Mass (FFM)		
∞Muscle wasting (< 16)	32	100
∞Non muscle wasting (> 16)	0	0

The mean of BMI before supplementation was increased after supplementation and it had an impact on the distribution of subjects based on BMI, which is decreased of number of subjects in underweight group was occured. We also found increased on FFMI as another anthropometry, but both of those improvement were not statistically significant. In contrast with CAT score as the quality of life indicator which decreased significantly and it indicated symptoms improvement after nutritional supplementation. Those parameter changes was shown in Table 2.

Table 2. Comparison of subject distribution pre and post Ophiocephalus extract supplementation

Variable	Pre		Post		p
	n	%	n	%	
Body Mass Index					
Mean (kg/m^2)		20,41±3,57	2 1,11±3,91		0,125
∞Underweight	13	40,63	4	12,5	
∞Normoweight	16	50,00	24	75,0	0,057
∞Overweight	3	9,38	4	12,5	
Fat Free Mass					
Mean 1		1,86±2,04	12,25±2,27 0		,186
∞Muscle wasting	32	100	29	90,63	0,083
∞Non muscle wasting	0	0	3	9,38	
CAT score					
Mean 1		7,91±7,81	11,25±8,28		**0,000**
∞CAT < 10	5	16,63	16	50	**0,000**
∞CAT ≥ 10	27	84,37	16	50	

The significant decrease of CAT score has further impact on the shift of COPD population distribution. Patients who previously were in more symptoms group (group B and group D population), after Ophiocephalus striatus extract supplementation shifted into less symptoms group (group A and group C population) as seen in Figure 1. The improved population shift was statistically significant with p value 0.037.
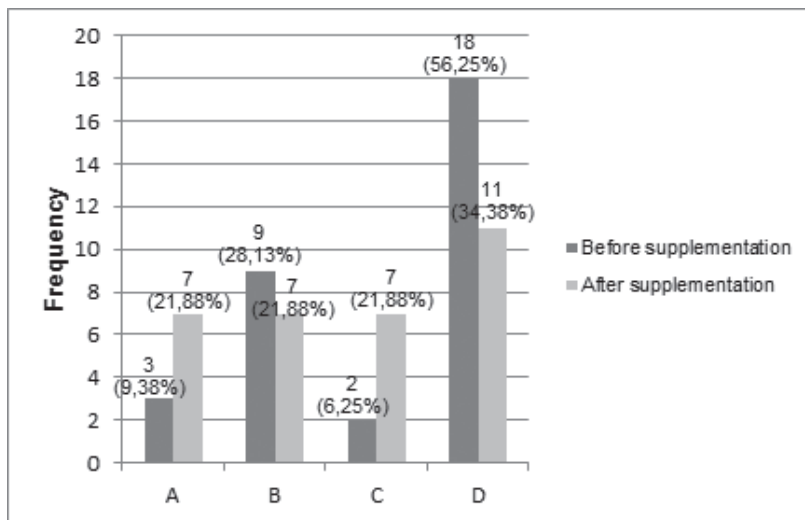
Figure 1. The effect of Ophiocephalus striatus extract supplementation on the change of COPD population

Table 3 shows a non-significant decrease of IL-17 and suPAR levels after administration of Ophiocephalus striatus extract. Lung function as measured by diffused lung capacity for carbonmonoxide (DLCO) also was not increase significantly.

Table 3. C hanges i n inflammatory c ytokine level (IL-17 d an s uPAR) and DLCO a fter Ophiocephalus striatus extract supplementation

Variable I	nitial value (pre)	Final value (post) p	
IL-17 level (pg/mL)			
Mean ± SD	20.521±14.526	17.841±9.658	0.275
Min – max 0	.3 – 54.3	2.5 – 42.8	
suPAR level (pg/mL)			
Mean ± SD	3.93±2.05	3.77±1.67	0.674
Min – max 0	.21 – 8.06 0	.84 – 7.31	
DLCO (% predicted)			
Mean ± SD	53.72±24.56	56.01±25.93	0.369
Min – max 1	7 – 101	14 – 127	

The relationship between inflammatory cytokine level (IL-17 and suPAR) and anthropometry parameter (BMI and FFM) was evaluated using correlation test and the results showed negative correlation which means the higher inflammatory cytokine level, the lower BMI and FFM value, indicating the more severe condition of muscle wasting. Similar negative correlation was also obtained in relationship between inflammatory cytokine level and diffused lung capacity, which indicates increase of inflammatory cytokine level will worsen the diffused lung capacity. Meanwhile, when associated with CAT score as quality of life indicator, possitive correlation was found with both IL-17 and suPAR levels. It suggests that elevated levels of inflammatory cytokine will increase CAT score that indicate decline quality of life.

DISCUSSION

Subjects distribution by the mean age was 62.72 years old with the most is in group over 60 years old. Research data from Persahabatan Hospital Jakarta showed the average age of COPD patients was 68.27 years old.[11] Meanwhile, the research conducted in Saiful Anwar General Hospital Malang by Rahayu et al in 2016 showed the average age of COPD patient was 66.08 years old with the most is in the range 61-70 years old.[12] Minimum age in inclusion criteris is 40 years according to the prevalence of COPD. While the consideration to limit the age of 65 years as the maximum age is to avoid bias caused by muscle wasting that occurs due to aging process.

All of the subjects were male (100%) and it is in line with the study from Kartikaningsih et al., 2015 and Rahayu et al., 2016 in Malang. Data research from National Health and Wellness Survey USA in 2010 found that 57.6% of COPD patients were male.[12,13] This is related to smoking habits as one of COPD risk factor which is more prevalent in males than females, ie the prevalence of smoking habits in men ranges from 27-73% which is much higher than women who are only 2-21%.[14]

Cigarette smoke, air pollution, and recurrent lower respiratory track infection are the risk factors of COPD, but cigarette smoke both in active and passive smoker is the major causative factor in COPD, especially in developing countries including Indonesia. All of the subjects had history of smoking and the majority was heavy smoker according to Brinkmann Index. In developing countries, especially in middle to lower income people, cigarettes acounts for more than 65% of household.[15]

Most of the subjects was in group D of COPD population. Symptoms severity based on CAT score and

mMRC contributes to determine COPD population, and it depends on degree of lung damage associated with smoking habit. There is a relationship between the degree of smoking and the severity of COPD, ie moderate and heavy smokers are 8 times more prone for severe COPD than light smoker.[1]

According to anthropometry parameter, most of study subject had normal BMI although subjects who were underweight was quite a lot (40.63%). Study on COPD population in Africa showed no significant correlation between BMI and COPD symptoms, CAT score, and frequency of exacerbation which all determine COPD population. BMI is associated with comorbidities in COPD patient. Normoweight patients generally has hypertension comorbidity, meanwhile underweight and overweight patients tend to have coronary heart disease and diabetes mellitus.[16] Most of the study subjects had no comorbidity, but 2 subjects had hypertension and both of them were in normoweight category.

Despite having normal BMI, all subjects experienced a decreased body mass proven from Fat Free Mass (FFM) which was under 16. Approximately 60-80% of muscle cell mass consists of FFM, so that better using FFM as reduced body mass parameter because FFM may already decrease even though no decrease in body weight. This theory is in line with this study subjects' characteristic, whose most of BMI was normoweight and may not experienced weight loss, but entirely has decrease of muscle mass. Cigarettes smoke play a role in decrease of skeletal muscle mass. Eight weeks of cigarettes smoke exposure results in altered myosin and muscle mitochondria function, increase of protelolysis regulator, and reduce muscle cell contractility. It occurs in all smoker, either COPD patients or asymptomatic ones.[17]

Twelve weeks administration of Ophiocephalus striatus extract results in increase of BMI. The number of malnourished subjects whose BMI was underweight decreased, while the number of normoweight and overweight subjects increased. Study result from Kumar, 2014 found significant increase of BMI after 3 weeks administration of commercial nutritional supplementation 500 ccal/day or additional nutritional therapy in the form of high protein diet and 20% carbohydrates for 6 weeks. That increase of BMI was not found in stable COPD patient who only consume usual daily food without any nutritional therapy intervention.[18] This suggests that any kind of nutritional therapy administered to COPD patient has benefit in icreasing BMI which further reduces mortality, in view of association between low BMI and mortality in respiratory disease.[4]

In elderly COPD population, sarcopenia is accelerated by as much as 30% due to additional skeletal muscle loss process due to aging process. The insignificant increase of FFM in this study was different from study result by Sugawara in 2010 that combined administration of nutritional supplementation with low impact physical exercise for 12 weeks, then found significant increase of FFM after that kind of intervention.[19] Anthropometric changes are not only influenced by the nutritional status, but also by the physical exercise performed. Exercise training is able to induce anabolic response in COPD patients, increase muscle mass as measured by FFM, and furthermore contribute to functional improvement. In patients who experienced body mass composition depletion, a combination of nutritional therapy and physical exercises is preferred than giving the intervention separately. Similar to COPD patients with muscle wasting who only received physical exercise without nutritional supplement, who showed insignificant FFM. These results suggest the need of more comprehensive management in depleted body composition patient to reach FFM improvement.[20]

The COPD Assessment Test (CAT) is a questionnaire widely used in daily clinical practice because it's brief, easy to used, and represent patient's condition comprehensively. This study result showed significant improvement of quality of life in stable COPD patient after 12 weeks of nutritional supplementation as

assessed by the improvement of the mean CAT score. In a meta-analysis study in malnourished stable COPD patients, nutritional supplementation significantly improved their quality of life and their ability to perform their daily life routines, as well as increasing muscle strength, and cognitive function.[18]

Administration of fish oil capsules containing eicosapentaecoic acid (EPA) and docosahexaenoic acid (DHA) of 2 grams / day for 9 weeks has been shown to decrease IL-17, IL-10, IL-1β, and TNF-alpha, IL-17. Similarly, supplementation of 3.000 mg of omega-3 for 8 weeks decreased IL-17, C-reactive protein, and creatine kinase level significantly. In contrast with this study result that showed insignificant decrease of IL-17 that could happened because the different type and content of nutritional supplementation.[20,21] More over, in patient with pulmonary cachexia, response to nutritional supplementation is less satisfied due to severe degree of inflammation that has occured before. This study result is in accordance with Broekhuizen et al., that showed no improvement in TNF-α and IL-7 levels after 8 weeks supplementation of Polyunsaturated Amino Acid (PUFA).[22]

Acute inflammatory conditions will increase levels of proinflammatory cytokines, including suPAR, which subsequently lead to tissue remodeling, cell migration and proliferation, coagulation, and proteolysis. suPAR also plays a role in the occurrence of fibrosis in the airway due to chronic inflammation, which is associated with the severity of COPD and other chronic diseases.[23] Providing high protein nutrition (1.7 grams/kg BW/day) in acute condition patient such as SIRS coupled with energy supplementation equivalent to 18.8 grams protein/day has been shown to reduce suPAR levels significantly.[24] In contrast, there was insignificant decrease of suPAR levels in this study after adminisration of Ophiocephalus striatus extract enriched in protein, omega-3 and amino acids. That could happened because subjects in this study is in stable condition, while suPAR increases especially in acute exacerbation.[25]

Decrease of body mass associated with lung function, decrease of respiratory muscle strength, and diffused lung capacity.[10] Ophiocephalus striatus extract administered for 3 months in this study did not showed significant improvement in DLCO. This study aggrees with Thomashow et al that provide PUFA omega-3 for 6 months and obtained no improvement in lung function as measured by FEV1 and DLCO. It could happened due to altered lung function, especially airflow limitation occurs in COPD is irreversible, so the therapy given is only slow its progression and not improved lung function.[20,21] Research using diffusing capacity as parameter of lung function has not been widely performed in Indonesia because it is not a routine examination performed on COPD patients like spirometry and not all center have such examination facility. All correlation test showed no significant realtionship between all variables examined. It could happened because there are many pathways play a role in muscle wasting, so IL-17 and suPAR are not the only cytokines that play a role in COPD pathogenesis or muscle wasting. The other cytokines that involve are TNF-α, TGF-β1, IL-1β, IL-6, and IL-8, so we can not determine the relationship only through 1 cytokine.[5], This study limitation were : (1) All subjects were male so we can not evaluate the muscle wasting condition in female COPD patients, (2) Intervention given only by nutritional supplementation without physical exercise, and no control over subjects' daily physical activity, (3) Lung diffusion capacity examination is a new examination for COPD patients in our center and the manuver is difficult, especially in elderly patiens with severe grade of COPD.

CONCLUSION
Significant improvement of quality of life as assessed by CAT score occured after 12 weeks administration of Ophiocephalus striatus extract in COPD patients with muscle wasting. However, the improvement of IL-17 and suPAR levels, and DLCO was not significant. There was no significant correlation between the

level of inflammatory cytokine (IL-17 and suPAR), diffused lung capacity, CAT score, and anthropometry parameter (BMI and FFM).

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CLINICAL CHARACTERISTICS OF PULMONARY AND EXTRAPULMONARY TUBERCULOSIS PATIENTS: A STUDY OF INDONESIAN POPULATION

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ABTRACT

Introduction:
The 2017 Global Tuberculosis Report stated Indonesia as one of the countries with high tuberculosis (TB) burden rate. The incidence of TB infection in Indonesia was estimated to be 1 million cases in 2016. Despite that, extrapulmonary tuberculosis (EPTB) had not been receiving much attention. The diagnosis of EPTB is more difficult and certain types had worse prognosis. Therefore, the aim of this study is to investigate the clinical profiles of patients with EPTB compared to the patients with pulmonary TB (PTB).

Methods:
A cross-sectional study was conducted on 112 TB and EPTB patients diagnosed in a tertiary hospital,CiptoMangunkusumo National General Hospital in Jakarta. Characteristic demography and clinical profiles were obtained from medical records. Bivariate analysis was performed to compare clinical characteristics between TB and EPTB patients.

Results:
The prevalence of patients with PTB was 73 (65.2%), EPTB was 23 (20.5%), and mixed TB infections (PTB+EPTB) was 16 (14.3%).The most common site of EPTB was lymph nodes (9.8%), followed by vertebrae (8.9%) and peritoneum (7.1%). EPTB and mixed infections were more commonly found in young patients (median age 36.5 and 27.0 years old respectively, $p = 0.004$) and married patients (85%, $p = 0.037$). PTB was more commonly found in married(65.1%, $p = 0.037$), and patients with leukocytosis (35.6%, $p = 0.042$).

Conclusion:
Young age and being married were associated with EPTB infection. Leukocytosis and being married were associated with PTB infection. Further research is needed to confirm these results.

Background

Tuberculosis (TB) is an important global health problem. The 2017 Global TB report estimated that the total prevalence of tuberculosis around the world in 2016 was 10.4 million people, and 10% of those were infected with HIV.[1] About half of those cases occurred in developing countries, especially in South-East Asia region (45%). Although the incidence of TB decreased each year (about 2% per year), this decline is still not fast enough and mostly happened in European region. Surprisingly, Indonesia was ranked second amongst the top 5 countries accounting for 56% of the estimated TB cases. Indonesia is only ranked below India, and ranked above China, the Philippines, and Pakistan. The 2016 estimated incidence of TB in Indonesia is 1.020 million people. Although this might indicate an increase in prevalence, it might also reflect a better case notification rate.[1]

TB has a high morbidity and mortality rate. TB is the ninth most common cause of mortality in the world and placed first as the cause of mortality by a single infectious agent. The total estimated mortality in 2016 was 1.674 million people, and the rate of mortality in Indonesia was 47 per 100,000 people. These deaths

are preventable with early detection and treatment, because the treatment success rate around the world is 83%. Therefore, one of the targets in Sustainable Development Goals (SDGs) is to end the TB epidemic by 2030. However, these goals are complicated by several challenges that arise recently. The barriers to tuberculosis control include the increasing number of multiple drug resistant (MDR) and extensively drug resistant (XDR) tuberculosis, the high prevalence of latent TB, and the presence of comorbidities such as HIV infections and diabetes mellitus.[1]

About 10% of TB patients were infected by HIV in 2016, which contributed to 22% of the mortality. The estimated incidence of TB-HIV in Indonesia was 45,000 people. TB and HIV coinfection plays a synergistic role in disrupting the host's immune system. TB is the most common cause of AIDS-related deaths, and 99% of them occurred in developing countries.[1] It is estimated that about one-third of the world's population has latent TB infection and the risk of developing overt clinical TB disease is only 5-10% in immunocompetent adults. However, HIV infection can increase the risk of TB reactivation by about 20-fold. Moreover, TB can infect multiple organs in HIV patients, by hematogenous and lymphogenous spread causing extrapulmonary tuberculosis (EPTB).[2]

EPTB has not been receiving as much attention as pulmonary TB (PTB). However, EPTB accounted for 15% of the incident cases in 2016. The percentage of EPTB in Indonesia varies amongst different states, ranging from 0-19%.[1] This might be an underestimation, since the diagnosis of EPTB is often challenging.[3] There has not been a lot of studies elucidating the clinical profiles of EPTB compared with PTB in developing countries. A study in Nepal comparing the clinical characteristics of PTB and EPTB in 2008 observed that an age less than 25 years old and female gender were associated with EPTB.[4] Another study in CiptoMangunkusumo Hospital conducted between year 2008-2010 found that the prevalence of EPTB in HIV-positive patients was 32.95%; the majority of them were males from the age group 18-40 years old.[5] However, the data on the prevalence and clinical characteristics of EPTB in general TB population is still lacking. Therefore, this study aims to further determine the clinical profiles associated with EPTB in Indonesia compared to PTB.

Material and Methods
Patients and Data Collection
A cross-sectional study was conducted at tertiary hospital,CiptoMangunkusumo National General Hospital in Jakarta. A total of 112 TB and EPTB patients were undertaken from attending the Respiratory Outpatient Clinic, Department of Internal Medicine. Demographic characteristics and clinical profiles were obtained from medical records from January 2013 to December 2015. Inclusion criteria were the confirmed cases of TB and EPTB with comorbidities. Patients having other disorders such as COPD, asthma, lung cancer, and other lung diseases were excluded. Incomplete medical record were also excluded. In this study, PTB defined as all TB cases in lung, whereas EPTB defined as all TB cases outside the lung, including the pleura. Mixed infection defined as combination TB infection in pulmonary and extrapulmonary cases.

Statistical Analysis
The analysis was carried out using SPSS 24.0 version for Windows (SPSS Inc., Chicago, Illinois, USA). The results are presented in frequencies and percentages. Distribution of EPTB sites, demographic, and clinical characteristics of TB and EPTB patiens were obtained.The Kolmogorov-Smirnov test –the assessment of normal distribution of data, showed non-normal pattern. Hence, the appropriate non-parametric tests (Kruskal Wallis, Chi-square, Kolmogorov Smirnov test) followed by Tukey's post-hoc comparison test were used to compare the differences between PTB and EPTB.

Ethical Approval

This study received ethical approval from the Cipto Mangunkusumo National General Hospital Ethics Committee.

Results

There were 73 (65.2%) patients with PTB, 23 (20.5%) patients with EPTB, and 16 (14.3%) patients with mixed TB infections (PTB and EPTB). For EPTB infection, the most common sites were lymphatic (23.1%), spine (23.1%), and followed by peritoneum (20.5%), as presented on **Table 1.**

Table 1. Distribution of EPTB sites

Site	Frequencies (Percentages)
Lymphatic	9 (23.1)
Spine	9 (23.1)
Peritoneum	8 (20.5)
Meninges/brain	4 (10.3)
Endometrium	3 (7.7)
Kidney	2 (5.1)
Others (skin, mastoid, larynx, pleura)	4 (10.3)
Total	39 (100.0)

Demographic Characteristicsof PTB and EPTB Patients

EPTB and mixed infection were more commonly found in patients with younger age (median age 36.5 and 27.0 years old respectively, p = 0.004). For marital status, EPTB was commonly found in married patients (85.0%, p = 0.037). After conducting further post-hoc analysis, the age differences were significant between PTB-mixed infection and EPTB-mixed infection groups (p = <0.001 and 0.023 respectively).Meanwhile, the marital status differences were significant between EPTB and mixed infection group (p = 0.023). For other demographic characteristics, such as sex, education level, and occupation, there was no difference among the three groups.

Table 2. Demographic characteristics of PTB and EPTB patients

Characteristics		PTB (N=73)	EPTB (N=23)	Mixed (PTB+EPTB) (N=16)	p value
Age		43.0 (19–77)	36.5 (28–68)	27.0 (18–36)	0.004[a]*
Sex	Female	26 (35.6)	6 (26.1)	3 (18.8)	0.350[b]
	Male	47 (64.4)	17 (73.9)	13 (81.3)	
Education	Under secondary	14 (38.9)	7 (58.3)	3 (27.3)	0.868[c]

level	education				
	Secondary education and beyond	22 (61.1)	5 (41.7)	8 (72.7)	
Occupation	Not working	23 (40.4)	5 (35.7)	7 (50.0)	0.727[b]
	Working	34 (59.6)	9 (64.3)	7 (50.0)	
Marital status	Single	22 (34.9)	3 (15.0)	8 (57.1)	0.037[b]*
	Married	41 (65.1)	17 (85.0)	6 (42.9)	

[a] Kruskal Wallis test
[b] Chi-square test
[c] Kolmogorov-Smirnov test
* significant at $\alpha = 0.05$

Clinical Characteristics of PTB and EPTB Patients

For clinical characteristics, there were differences for diabetes mellitus and leukocytosis among the three groups. After conducting further post-hoc analysis, the difference was significant between PTB and mixed infection group for diabetes mellitus ($p = 0.048$). Meanwhile, the difference was significant between PTB and EPTB group for leukocytosis ($p = 0.013$). The clinical characteristics of this study subjects are presented on **Table 3**.

Table 3. Clinical characteristics of PTB and EPTB patients

Characteristics		PTB (N=73)	EPTB (N=23)	Mixed (PTB+EPTB) (N=16)	p value
Diabetes mellitus	No	56 (76.7)	22 (95.7)	16 (100.0)	0.004[c]*
	Yes	17 (23.3)	1 (4.3)	0 (0.0)	
Hypertension	No	57 (78.1)	21 (91.3)	14 (87.5)	0.659[c]
	Yes	16 (21.9)	2 (8.7)	2 (12.5)	
Anemia	No	66 (90.4)	21 (91.3)	13 (81.3)	1.000[c]
	Yes	7 (9.6)	2 (8.7)	3 (18.8)	
Leukocytosis	No	47 (64.4)	21 (91.3)	12 (75.0)	0.042[b]*
	Yes	26 (35.6)	2 (8.7)	4 (25.0)	
Pulmonary cavity	No	69 (94.5)	23 (100.0)	15 (93.8)	1.000[c]
	Yes	4 (5.5)	0 (0.0)	1 (6.3)	
Pleural effusion	No	63 (86.3)	22 (95.7)	14 (87.5)	0.987[c]
	Yes	10 (13.7)	1 (4.3)	2 (12.5)	

Positive acid-fast bacilli in	No	67 (91.8)	21 (91.3)	14 (87.5)	1.000[c]
Sputum	Yes	6 (8.2)	2 (8.7)	2 (12.5)	
Category of WHO regiment	1	61 (83.6)	17 (73.9)	14 (87.5)	1.000[c]
	2	12 (16.4)	6 (26.1)	2 (12.5)	
HIV status	No	68 (93.2)	23 (100.0)	15 (93.8)	0.985[c]
	Yes	5 (6.8)	0 (0.0)	1 (6.3)	
End-stage renal disease	No	69 (94.5)	23 (100.0)	16 (100.0)	0.696[c]
	Yes	4 (5.5)	1 (0.0)	1 (0.0)	

[a] ⬜r uskal Wallis test
[b] Chi-s⬜u are test
[c] ⬜ olmogorov-Smirnov test
* significant at $\alpha = 0.05$

DISCUSSION
Demographic Characteristics
In our study, patients with mixed infection (PTB + EPTB) were significantly younger than both PTB-only and EPTB-only patients. The range of age in mixed infection patients was in the young adult age group (median 27 years old, 18-36), whereas the range of age in both PTB- and EPTB-only groups was wider and encompassed the elderly. The median age of EPTB-only patients was slightly younger than those of PTB-only, and this difference is not statistically significant. A comparison study in Nepal observed that younger age especially age<25 years old is an independent risk factor for EPTB, which is similar to our study.[4] However, their definition PTB and EPTBis slightly different to ours in this study. They defined PTB as a TB infection that occurred only in intrathoracic area, including the pleura. The patients were said to have EPTB when there were infections in extrathoracic organs, even if the patients also have concurrent pulmonary involvement (which was categorized as mixed infection in this study).[4] However, this difference is not significant because only 1 patient in our study has pleural TB infection.

Our study also showed that the proportion of married patients in EPTB group was higher than that of the mixed infection group. The reason was unclear, perhaps because their spouse usually would notice PTB and had urged their partner to visit a doctor earlier before they developeda mixed infection. In contrast, the clinical presentation in early EPTB was more unclear. Currently, there were not a lot of studies comparing the risk of developing EPTB between single and married patients. However, a study by Crampin et al. reported that spouses of TB patients were in a high-risk group which should be screened for HIV and TB.[6] Further studies are needed to elucidate the role with regard to EPTB.

We did not find any difference in the proportion of gendersamong all three groups. The Nepal study reported that the male to female ratio in EPTB patients were significantly lower than that of PTB patients (1.07 vs. 2.209). They also performed multivariate analysis, which showed that female gender was associated with EPTB more than PTB.4 A retrospective study in North India, Spain, and Turkey also showed that the prevalence of EPTB was higher in female.[7-9] A large study involving 5414 TB patients in Taiwan also showed that females especially ≥45 years old had a higher rate of mixed infection.[10] The higher prevalence of EPTB in females is postulated to be caused by multiple factors, including lower access to health care, higher rate

of diabetes and malnutrition, and decreased sex hormone during menopause.[10-11] This difference in our result could be explained by the imbalanced ratio of male to female ratio in our study (about 2:1).

Clinical Characteristics

Our study found that diabetes mellitus was associated more to PTB than to mixed infection. The study from Nepal reported that diabetes was a higher independent risk factor for PTB than EPTB.[5]A study from North India also found higher comorbidities of diabetes and HIV infection with EPTB patients compared to PTB patients.[7] Studies have shown that the prevalence of tuberculosis is increased in poorly-controlled diabetic patients. TB in diabetic patients is associated with atypical radiology findings, longer time to sputum-culture conversion, and higher rate of treatment failure. Diabetes is associated with immune dysregulation, by impairing chemotaxis of monocytes, reducing interferon-γ production by T cells, and reducing lymphocyte proliferation, which can lead to reactivation of TB and possibly increasing the risk of dissemination.[12]Magee, et al conducted a retrospective cohort to assess the association between diabetes and EPTB.The study reported that diabetes was not associated with a higher probability of EPTB. However, there was a trend toward a higher proportion of all-cause mortality in EPTB patients with diabetes.[13] The result of our study also showed that diabetes was not associated either with EPTB or with mixed infection. However, the prevalence of diabetes is low and this study was not specifically designed to prove this hypothesis.

HIV is also associated with EPTB in several studies. A meta-analysis of 19 studies concluded that HIV infection was a risk factor of developing EPTB (OR: 1.31).[14] HIV causes CD4+ T cells dysfunction and reduction of TNF production, which leads to impaired granuloma formation and TB can spread by direct spread, hematogenous, or lymphogenous route.[2] Our study did not find significant association between HIV and EPTB, or between HIV and mixed infection, because the prevalence is low in our sample. Another significant characteristics in our study was leukocytosis, which occurred more often in PTB patients than in EPTB patients. This might also reflect the lower immune response in EPTB patients compared to in PTB patients.

Limitations

The first limitation of this study is the small sample size which contributes to prevalence of TB and EPTB patients and comorbidities. In addition, non-normal distribution pattern of demographic charateristics also weakens the statistical power of this study. Moreover, the data collection of this study is retrospective and documentary, which may generate information bias, with the loss of some medical records.

Conclusion

Younger age and being married were associated with EPTB infection. Diabetes mellitus and leukocytosis were associated with PTB infection. Further research with a larger sample size is needed to confirm these results

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INDIVIDUAL FACTORS IN RELATION TO THE VITAL LUNG CAPACITY AMONG WELDERS OF METAL WORKING SECTION AT PT. F FORMAL SECTORIN 2018

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ABTRACT

Welding is one of the industrial processes that potentially causes air pollution in the work environment, in the form of welding fumes and gases. In addition to work environment factors, individual factors such as age, nutritional status, working period, duration of exposure, use of personal protective equipment (PPE) masks, smoking habit and exercise habit also play an important role in the vital lung capacity (VLC) of workers exposed to dust. VLC is a lung volumes measurement to determine the presence or absence of pulmonary function disorders. The aim of this research is to investigate individual factors associated with VLC among welders of metal working section at PT. F, formal sector in 2018. This research uses observational analytic method with cross sectional design, with 42 samples according to the criteria. Data collection procedure was done by conducting interviews, measuring VLC using a Spirometer PC-10 and measuring body mass index (BMI). Data analysis was performed with Chi-square test, continued by multivariate logistic regression analysis.

The result shows that 14 (33,3%) of 42 welders have pulmonary function disorders. The final result shows that the 3 most influencing individual factors toward the VLC are: uses of PPE masks (p=0,000 OR=13,954), working period (p=0,026 OR=8,835) and duration of exposure (p=0,002 OR=5,881). In conclusion, welders and PT. F are suggested to improve preventive efforts with more attention of the above three factors, in order to reduce occupational lung disease.

Keywords : Individual factors, vital lung capacity, welders, occupational lung disease, spirometry

INTRODUCTION

Indonesia's economic growth is considered poised to improve in Southeast Asia as the rapid growth of industrial sector[1]. Welding is one of the industrial processes that potentially causes air pollution in the work environment, in the form of welding fumes and gases. There are several welding effects to its welders such as bronchitis, respiratory tract infection and irritation and metal fumes fever[2]. According to the Law of Republic of Indonesia Number 36 Year 2009 concerning Health, article 165 that says 'Management of the workplace shall be obligated to make all health efforts through prevention, increase, treatment and recovery for workers'[3], therefore, risky workers is highly recommended to check their vital lung capacity (VLC) in order to prevent pulmonary function disorders or occupational lung disease.

Many studies have been done with varying results concerning factors related to VLC among workers exposed to dust. In Prasetyo's study[4], uses of PPE masks, smoking habit, age and working period were associated with VLC,however, Budiono[5] reported that there was no associated between those four factors with VLC.In addition, there is also a gap between the relationship of other individual factors, such as nutritional status, duration of exposure and exercise habit, so further research is needed by including these seven individual factors.

PT. F is one of the formal sector industries, which in the process, there are some welding work on the metal working section. The top priority in the formal sector industry is occupational health and safety program

(K3) that distinguishes it from the informal industrial sector, thus can be seen that the work environment of PT. F does not potentially pose a health risk to the workers.Yet there are some health complaints of welders experiencing respiratory problems. Based on the above description, we are interested to investigate individual factors (age, nutritional status, working period, duration of exposure, uses of PPE masks, smoking habit and exercise habit) associated with VLC among welders of metal working section at PT. F, formal sector in 2018.

SUBJECTS AND METHODS
This cross-sectional study was conducted among welders of metal working section at PT. F formal sectorin March 2018. Based on the sample size calculation using Lameshow formula, 42 welders were recruited as subjects[6]. The sampling technique used was consecutive sampling.The subjects were consecutively selected in order of appearance according to the inclusion criteria, the sampling process comes to an end when the total number of subjects were reached[7].

The inclusion criteria were: males, agreed to become the research subjects and agreed to fill the informed consent form. The exclusion criteria were: welders withpast medical history suggestive of asthma, chronic obstructive pulmonary disease, chronic cough, tuberculosis and lung cancer.

Data collection procedure was done by conducting interviews, measuring body mass index (BMI) andmeasuring VLC using a Spirometer PC-10 that has been calibrate.Maneuver were performed in a standing position with a nose clip and disposable mouthpiece. Data analysis was performed with Chi-square test, continued by multivariate logistic regression analysisenter method. This research was approved by ethics committee of Faculty of Medicine, Universitas Pembangunan Nasional "Veteran" Jakarta.

RESULTS
Univariate Analysis Results
Table 1 presents VLC interpretation of all subjects. Unfortunately, there was no subjects with obstructive lung disease in this research. So that, spirometry test result for VLC measurement were only classified into normal and restrictive lung disease.The result shows that 14 (33,3%) of 42 welders have pulmonary function disorders of restrictive lung pattern. Restrictive lung disease is characterized by decrease forced vital capacity (FVC)<80% predicted[8].

Table 1. Spirometry measurement results

No.	VLC	Frequency (f)	Percentage (%)
1.	Restrictive	14 3	3,3%
2.	Normal 2	8	66,7%
J	umlah	42 1	00%

(Source: Primary data, 2018)

Table 2 presents individual factors (age, nutritional status, working period, duration of exposure, uses of (PPE) masks, smoking habit and exercise habit)of all subjects.

Table 2. Individual factors distribution

Individual Factors	Frequency N = 42	Percentage N = 100%
Age		
≥ 35 years 1	6	38,1%
< 35 years	26	61,9%
Nutritional status		
Abnormal 1	7	40,5%
Normal 2	5	59,5%
Working period		
≥5 years 1	7	40,5%
<5 years 2	5	59,5%
Duration of exposure		
≥8 hours/day 1	9	45,2%
<8 hours/day 2	3	54,8%
Uses of PPE mask		
Intermittent use 1	8	42,9%
Always use 2	4	57,1%
Smoking habit		
Smoking 2	7	64,3%
Nonsmoking	15	35,7%
Exercise habit		
Nonexercise	22	52,4%
Exercise	20	47,6%

(Source: Primary data, 2018)

Bivariate Analysis Results

Table 3 presents that most subjects with age < 35 years had normal VLC interpretation (76,9%), but the result shows that there was no relation between age and VLC (p-value>0,05).

Table 3. Relation analysis between age and VLC

Age	Vital lung capacity T				otal	*P*
	Restrictive		Normal			
	N	%	N	%	N	
≥ 35 years	8	50,0 8	5	0,0	16	
< 35 years	6	23,1 2	0	76,9 2	6	0,072
Total	14 3	3,3	28 6	6,7	42	

(Source: Primary data, 2018)

Table 4 presents that there was no relation between nutritional status and VLC (p-value>0,05). Out of 14 subjects with restrictive lung pattern, 7 subjects were from abnormal nutritional status (underweight BMI < 18,5 or overweight BMI > 25) and the other 7 subjects were from normal nutritional status listed in the table.

Table 4. Relation analysis between nutritional status and VLC

Nutri-tional status	Vital lung capacity T				otal	P
	Restrictive		Normal			
	N	%	N	%	N	
Abnormal	7	41,2 1	0	58,8 1	7	0,374
Normal	7	28,0 1	8 7	2,0	25	
Total	14 3	3,3	28 6	6,7	42	

(Source: Primary data, 2018)

Table 5 presents that there was a relation between working period and VLC (p-value<0,05). Most subjects with restrictive lung pattern has working period ≥ 5 years (52,9%) and most subjects with normal VLC interpretation has working period < 5 years (80%).

Table 5. Relation analysis between working period and VLC

Working period	Vital lung capacity T				otal	P
	Restrictive		Normal			
	N	%	N	%	N	
≥5 years	9	52,9 8	4	7,1 1	7	0,026
<5 years	5	20,0 2	0	80,0 2	5	
Total	14 3	3,3	28 6	6,7 4	2	

(Source: Primary data, 2018)

Table 6 presents that there was a relation between duration of exposure and VLC (p-value<0,05). Subjects with duration of exposure ≥ 8 hours/day was more likely to has restrictive lung pattern (57,9%), while subjects with duration of exposure < 8 hours/day was more likely to has normal VLC interpretation.

Table 6. Relation analysis between duration of exposure and VLC

Duration of exposure	Vital lung capacity T				otal	P
	Restrictive		Normal			
	N	%	N	%	N	
≥8 hours/day	11 5	7,9 8	4	2,1	19	0,002
<8 hours/day	3	13,0 2	0	87,0 2	3	
Total	14 3	3,3	28 6	6,7	42	

(Source: Primary data, 2018)

Table 7 presents there was only 2 subjects that always use PPE masks experienced restrictive lung pattern. The result shows that there was a relation between uses of PPE mask and VLC (p-value<0,05).

Table 7. Relation analysis between uses of PPE mask and VLC

Uses of PPE mask	Vital lung capacity T				otal	P
	Restrictive		Normal			
	N	%	N	%	N	
Inter-mittent use	12	66,7 6	3	3,3	18	0,000
Always use	2	8,3	22 9	1,7 2	4	

Total	14	33,3 2	8	66,7 4	2

(Source: Primary data, 2018)

Table 8 presents that there was no relation between smoking habit and VLC (p-value>0,05). Out of 14 subjects with restrictive lung pattern, 11 subjects have smoking habit and the other 3 subjects does not have smoking habit.

Table 8. Relation analysis between smoking habit and VLC

Smoking habit	Vital lung capacity T				otal	P
	Restrictive		Normal			
	N	%	N	%	N	
Smoking	11 4	0,7	16 5	9,3	27	
Non-smoking	3	20,0 1	2	80,0 1	5	0,172
Total	14 3	3,3	28 6	6,7 4	2	

(Source: Primary data, 2018)

Table 9 presents that there was no relation between exercise habit and VLC (p-value>0,05). Most of subjects with normal VLC interpretation was from subjects that does not have exercise habits (80%).

Table 9. Relation analysis between exercise habit and VLC

Exercise habit	Vital lung capacity T				otal	P
	Restrictive		Normal			
	N	%	N	%	N	
Exercise	10 4	5,5	12 5	4,5	22	
Non-exercise	4	20,0	16 8	0,0	20	0,081
Total	14 3	3,3	28	66,7 4	2	

(Source: Primary data, 2018)

Multivariate Analysis Results

Multivariate analysis in this research was done by taking independent variables that have relation with dependent variable from bivariate analysis results. Continued by multivariate logistic regression analysisenter method.

Table 10 present odds ratio values which used to determine the strength of the relation between independent variable and dependent variable.

No V	ariable	P-value	Oddsratio (OR)
1	Workingperiod 0	,043 8	,835
2	Durationofexposure	0,108	5,881
3	Usesof PPE mask	0,013	13,954

DISCUSSION

Welding fumes can induce adverse respiratory irritation.Irritation caused by welding fumes might appear as emphysema, obstructive disorder, and pulmonary fibrosis. Pulmonary fibrosis will lead to the decreased

of lung compliance capability and the decreased of all lung volumes including VLC.The lungs workload will become heavier in order to overcome lung elastic recoil, causing rapid shallow breathing. It may result in alveolar hypoventilation and the inability to maintain normal blood gas pressure and will lead to restrictive lung disorders as the final result[2].

In the present study, there were 66,7% of subjects with normal VLC interpretation, while subjects with pulmonary function disorders were 33,3%.It should be noted that the formal sector work environment was in accordance with prevailing standards and dust levels was not exceed the threshold limit value (TLV), so the risks that may arise was small.

However, other factors such as age and nutritional status might increase the risk of pulmonary function disorders in welders. At the age of 25 to 35 years, lung function remains steady with very minimal change and starts declining thereafter[9], but in our research this factor has almost no influence on VLC. As well as nutritional status, although nutrition has an important role to VLC as an antioxidant to prevent free radicals[5], in bivariate analysis results shows that there was no relation between nutritional status and VLC, similarly to earlier report by Gidikova et al. that there was no correlation between the measured expiratory volumes and body mass index (BMI) or age was found[10].

Working period is the length of employee work (year) in one company environment calculated from the beginning of work until the research took place[11]. In Prasetyo'sandPutra'sstudies, welders with work period longer than 5 years showed a significant reduction in the values of VLC[4, 12]. Therefore, our findings are in accordance with those studies.This can happen because the longer a person is at work, the more he or she is exposed to the hazard posed by the work environment[13].

Duration of exposure is defined as the number of working hours per day or per week.Univariate analysis result showed that most of welders had less than 8 hours working hours per day, which was 54,8%.The number of working hours per day was in accordance with the Manpower Act No.13 of 2003 article 77 which stipulates 8 working hours in one day and 40 working hours in one week in the case of the working periods being 5 days in one week[14].But there were still 45,2% welders who had working hours more than 8 hours per day, due to the overtime work or the target pursuit.

Similar to our research, Deviandhokofound correlation between duration of exposure (≥8 hours/day) and pulmonary function disorders[2]. The number of welder's working hours causes different intensity of exposure and the amount of welding fumes and gases inhaled by each welder, so that welders with long working hours potentially inhale more fumes and gases[12].

Using a mask as personal protective equipment (PPE), may also help to reduce welding fumes and gases exposure towards welder. However, our univariate analysis findingsshow that there were 42,9% welders with intermittent uses of PPE masks. Uncomfortable isthe main reason why welders are not always use PPE masks and only use itif there is field evaluation, although PT. F has provided full PPE with various sizes. It is known that welders of metal working section at PT. F formal sector were lack of self-awareness in using PPE masks. Our bivariate analysis findings show that there was a relation between uses of PPE masks and VLC, we also found 66,7% welders with intermittent uses of PPE masks has restrictive pattern of lung function. This result is in accordance with Prasetyo'sstudy[4].

Smoking habit in decrease values of VLC is significant factors in some researches[4,10], but in our research,

smoking habit in welders had no significant effect on their VLC values (p-value=0,172). This could be possibly due to the largest percentage were light smoker in this research. It is well known that smoking can interfere the effectiveness of respiratory defense mechanisms, in addition to cigarette smoke that can stimulate mucus production and reduce ciliary movement of the respiratory system[15]. Smoking habit in this research was calculated using Brinkman Index, which is defined as number of cigarette smoked per day times smoking years.

The last factor studied in this research was the exercise habit. There was no relation between exercise habit and VLC in our bivariate analysis result, by contrast, Rasyid's study has reported there was significant correlation between exercise habit and VLC[16]. Nevertheless, subjects with nonexercise habit experienced pulmonary function disorders (45,5%) greater than subjects with exercise habit (20,0%). Pulmonary function and exercise have reciprocal relation, impaired lung function may affect exercise ability, by contrast, physical exercise may improve lung function[16]. Based on these explanation, although the result shows that there was no relation between exercise habit and VLC among welders of metal working section at PT. F formal sector, welders are suggested to started exercising regularly to improve their health.

Multivariate analysis result presents 3 most influencing individual factors toward VLC. The first is uses of PPE masks (OR=13,954). Welders with intermittent uses of PPE masks has 13,954 times higher risk of pulmonary function disorders than welders with always uses of PPE masks. The second is working period (OR=8,835). Welders with working period ≥ 5 years has 8,835 times higher risk of pulmonary function disorders than welders with working period < 5 years. The third is duration of exposure (OR=5,881). Welders with duration of exposure ≥ 8 hours/day has 5,881 times higher risk of pulmonary function disorders than welders with duration of exposure < 8 hours/day.

There was limitation that should be noted in this research because this research uses cross sectional design.

CONCLUSION
In summary, there were14 (33,3%) of 42 welders have pulmonary function disorders. Uses of PPE masks was a leading individual factor for the decrease of VLC among welders of metal working section at PT. F formal sector, followed by working period and duration of exposure. On the other hand, other individual factors such as age, nutritional status, smoking habits and exercise habits has no significant relation towardsVLC in this research.

PT. F are suggested to improve preventive efforts such as conduct regular safety talk to increase welder's education about occupational health and safety (K3), tighten field supervision and do reward and punishment system to improve welders discipline in using PPE masks.

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THE DIFFERENCE OF ALLERGEN TYPES IN ALLERGIC RHINITIS PATIENTS WITH AND WITHOUT ASMA BASED ON THE SKIN PRICK TEST EXAMINATION

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Abstract Background: Allergic rhinitis (AR) could occur with or without asthma. To be able to perform the management, both in educating and in avoiding exposure to allergens which exacerbate the disease (avoidance), the knowledge of the type of allergen must be ascertained. Skin prick test (SPT) is an advantageous diagnostic tool due to its simplicity, safe, and quick result as well as for its sufficient sensitivity. Material and method: This was a cross-sectional analytic study which consisted of 40 study samples. Twenty samples were classified as allergic rhinitis without asthma while twenty others classified as allergic rhinitis with asthma. The study was conducted on ENT Head and Neck clinic and COPD/Asthma clinic of Adam Malik General Hospital Medan. Demographic data and allergen types were analyzed. In addition, correlation test was performed between the classification of AR and the severity of asthma using Spearman's correlation test with $\alpha=0.05$(95% CI). Result: The age distribution of both groups was the same but with different proportions. The most positive allergen types between the groups were house dust mite but the type of house dust mite was different between the two groups. Of all the patients, 16 (80%) were women. The most common type of allergen in AR without asthma was D. fariane (27%), while Tropicalis blomia (29.3%) was predominant in AR with asthma. The spirometry result of AR with asthma group was worse than AR without asthma group. Conclusion: This study demonstrates the importance of education and counseling to avoid house dust mites' exposure which trigger the incidence of allergic rhinitis in order to prevent asthma attacks.

BACKGROUND

The management of Allergic Rhinitis (AR) is highly difficult due to its long-term treatment, high-cost, and patient's compliance.1 The most effective approaches for the management of AR is avoiding exposure to allergens which exacerbate the disease (avoidance). Determining the allergens required identification which can be done by Skin Prick Test (SPT).[2]

Skin prick test (SPT) is an advantageous diagnostic tool due to its simplicity, safe, and quick result as well as for its sufficient sensitivity in diagnosing allergic conditions. However, often it wasn't feasible in health care facilities,[3] although patients with AR and asthma often attends the primary health care centers. Therefore, studies are needed to determine the causative allergens of AR and asthma; thus supporting the clinicians in primary health settings to provide education for the management of these disorders.

This study aims to define the difference of allergens in patients with allergic rhinitis and asthma compared with allergic rhinitis without asthma based on SPT.

MATERIALS AND METHODS

This was a cross-sectional analytic study which consisted of 40 study samples, divided into 2 groups. Twenty samples were classified as allergic rhinitis without asthma while twenty others classified as allergic rhinitis with asthma who come to ENT Head and Neck clinic, rhinology/allergy immunology division and COPD/Asthma clinic of Adam Malik General Hospital Medan. The study conducted from October-December 2017. The inclusion criteria were:(1) patients who diagnosed with AR confirmed with positive SPT, (2) patients diagnosed with asthma and AR based on spirometry and positive SPT, (3) those who willing to be

included in the study and signed the informed consent. The exclusion criteria including relapsing asthma attacks during the examination and those who refused to continue the study.

After undergoing a routine ENT examination, SPT examination was performed. The patient must be made sure to not consume any antihistamine drugs at least 2-7 days prior and not having asthma attacks in the last 24-hours. Following positive SPT, spirometry examination was performed by a pulmonologist.

SPT is an allergenicity test using allergen extract to diagnose allergenic response against administered allergens on the volar region to determine the presence of IgE-mediated responses. In SPT (Stallergen, France), there are seven kinds of allergens used including a variety of house dust mites (Tropicalis blomia, D. pteronyssinus, and D. fariane), Grass Bermuda, Cockroach B Germanic, Cat, and Dog. Positive SPT is defined as a formed lump with $\geq$ 3 mm in diameter.

RESULTS
All subjects were asked for the main complaint and undergo a physical examination, SPT, and spirometry. The most common complaints experienced by AR patients without asthma were sneezing in 18 (90%) patients, nasal congestion in 13 (65%) patients, and runny nose in 10 (50%) patients, while in AR with asthma were sneezing in 19 (95%) patients and runny nose in 12 (60%) patients. From physical examination, livide and edematous inferior turbinate were higher in AR without asthma in 13 (65%) patients while in AR with asthma, livide and eutrophic inferior turbinate was found in 15% (75%) patients. From spirometry results, AR patients with asthma had FEV1 and PEF worse than AR without asthma (Table 1).

Table 1 The results of examinations.

Examination Results	AR n (%)	AR + Ashtma n (%)
∞ **Main complaint**		
- **Sneezing**	18 (90)	19 (95)
- **Runny nose**	10 (50)	12 (60)
- **Nasal congestion**	13 (65)	5 (25)
- **Itchiness**	5 (25)	5 (25)
∞ **Physical examination**		
- **Livide and edematous inferior turbinate**	13 (65)	5 (25)
- **Livide and eutrophic inferior turbinate**	7 (35)	15 (75)
∞ **SPT**	20 (100)	20 (100)
∞ **Spirometry**		
- **FEV$_1$ > 80%**	4 (20)	4 (20)
- **FEV$_1$ 60-80%**	14 (70)	8 (40)
- **FEV$_1$ < 60%**	2 (10)	8 (40)
- **PEF > 80%**	19 (95)	14 (70)
- **PEF 60-80%**	1 (5)	3 (15)
- **PEF < 60%**	0 (0)	3 (15)

From 40 studied subjects, females were predominant with 16 women (80%) in each group. Meanwhile, the most common age groups were 15-24 years in both groups with different proportions; in AR without asthma group, there were 12 (60%) patients while in the AR with asthma group there were 8 patients (40%). The majority of patients had a history of atopy in family members with 16 (80%) patients in the AR with asthma and 14 (70%) patients in AR without asthma.

In this study, the most common allergen types between the groups were house dust mite but the type of house dust mite was different between the two groups. The most common type of allergens in the AR without asthma were D. fariane (27%), followed by D. pteronyssinus and Tropicalis blomia at 25%. In contrast, Tropicalis blomia was the most common allergen in the AR with asthma at 29.3%, followed by D. pteronyssinus and D. fariane at 25.8%. These three variants were the most common types of allergens from SPT results (Table 2).

Table 2 Distribution of frequency of the allergen types in AR patients with and without asthma.

Types of allergen	AR n (%)	AR + Asthma n (%)
Grass bermuda	3 (6,2)	2 (3,4)
Tropicalis blomia	12 (25)	17 (29,3)
Cockroach B Germanic	5 (10,4)	4 (6,8)
D. pteronyssinus	12 (25)	15 (25,8)
D. fariane	13 (27)	15 (25,8)
Cat	2 (4,1) 2	(3,4)
Dog	1 (2)	3 (5,1)

The AR withasthma group, a total of 20 patients, classified by AR classification (according to ARIA) and asthma severity (according to GINA classification). Table 3 mostly shows patients with moderate to severe persistent AR, 57.1% classified as mild asthma, 14.3% (1 person) moderate asthma, and 28.6% (2 persons) severe asthma.

Table 3 The association between AR classification (according to ARIA) with asthma severity (according to GINA classification) in AR patients with asthma.

AR classification (according to ARIA)	Asthma severity (according to GINA)			Total
	Mild Asthma n (%)	Moderate Asthma n (%)	Severe Asthma n (%)	
Mild Intermittent	4 (80)	0 (0)	1 (20)	5 (100)
Moderate-severe intermittent	1 (50)	0 (0)	1 (50)	2 (100)
Mild persistent	3 (50)	0 (0)	3 (50)	6 (100)
Moderate-severe persistent	4 (57,1)	1 (14,3)	2 (28,6)	7 (100)
Total	12 (60)	1 (5)	7 (35)	20 (100)

The result of statistical analyses between ARIA and GINA using Spearman correlation test showed that a p-value = 0,657; it could be concluded that there's no significant correlation between the classification of AR with the severity of asthma (Table 4).

Table 4 Spearman correlation test results.

Association between AR and asthma	N	p-value
AR classification according to ARIA	20	0,657
Asthma severity according to GINA	20	

DISCUSSION

Allergic rhinitis (AR) is a common immunologic disease. AR isn't lethal, but its symptoms could affect one's wellness and lower their quality of life. The AR could lead to the development of asthma. Several studies have shown that AR and asthma often occur concomitantly.

In this study, the most common complaints encountered by AR patients with and without asthma were sneezing. On physical examination, livide and edematous inferior turbinate were more common in AR patients without asthma, in contrast, livide and eutrophic inferior turbinate were more common in AR with asthma. Rafi et. al. (2015) also found that the most common AR symptoms encountered by patients were sneezing with 93.24% and livide inferior turbinate were found in all subjects.[4] Sneezing in AR is a symptom of a rapid-phase allergic reaction. This reaction could last up to an hour after contact, with peaks at 15-20 minutes after exposure; this is linked with mast cell degranulation resulting in histamine release. The released histamine stimulates the H1 receptors on Vidian nerve ending, causing itchiness and sneezing.[5] Utama (2010) suggest that the interaction of IgE with mast cells or basophils, trigger the release of mediators such as histamine, leukotriene, prostaglandin, and platelet activating factor (PAF), leading to plasma leakage from the blood vessels and dilatation of arterial anastomosis causing edematous turbinate.[1]

From the demographic features, women were the most common in both groups. Similar with a study reported by Ismayani (2017), women were more likely to develop AR at 78.04% and by Bey (2015) where women are more often to visit asthma clinic at 59.6% rather than men.[6,7] Psychological factor explained how this could happen. Women are generally susceptible to anxiety against disease manifestation. The caliber of airways of women also smaller than men's.[8] In this study, AR and asthma were more common in 15-24 years' age group with different proportions. Shin et. al. (2012) also found that the most common age group of AR with and without asthma were in 15-24 years.[9] Eighty percent cases of AR occur before 20 years or during productive years. This could be explained that these age groups are commonly more exposed to aeroallergen with poorly ventilated work environments, school areas, or dusty study place.[10,11] Harsono et. al. (2007) suggested that the risk of AR was greater in patient with family history of atopic in both parents than only one of the parents, but it must be considered that incidence of AR was multifactorial. People without a family history of atopy could also develop AR.[12]

Almost all studies which use SPT found that the house dust mites were predominant but with different allergen types. Shin et. al. (2012) found that the most common aeroallergens from the study population in the AR with asthma group in Korea were house dust mite with allergen type of D. fariane in 56.4%, followed by D. pteronyssinus in 46.3% compared with AR group or asthma group. This could be caused by high humidity and temperature in Korea which is very suitable for house dust mite.[9] In contrast, the average temperature in Indonesia is around 23-30°C with humidity of 68% which allows the house dust mites and cockroaches to properly grow.[1] House dust mites such as D. fariane and D. pteronyssinus, live by consuming peeled skin and most often found on mattresses and pillows made from cotton or carpets that never cleaned or dried. It is advised to clean the blanket and carpet at least once a week and to add 0.03% benzyl benzoate to eliminate them.[1,13]

In this study, there was no significant relationship between the classification of AR and the severity of asthma in 20 patients with AR and asthma. Nevertheless, in moderate to severe persistent AR classification, there was three severity of asthma: mild asthma, moderate asthma, and severe asthma. Epidemiologic data showed a close relationship between AR and asthma. Various studies showed that 78-94% of asthmatics in adolescents and adults also suffered from AR and 38% of people with AR also suffered from asthma. In addition, patients with AR have a higher sensitivity to bronchus than healthy people. Therefore, controlled AR could prevent the onset of asthma attacks.[12]

CONCLUSION
The most effective AR management is to avoid allergens exposure which trigger the disease. Providing education and counseling on how to avoid allergens exposure to house dust mites could control allergic rhinitis and prevent the onset of asthma attacks.

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ABTRACT POSTER

PNEUMOTHORAX, PNEUMOMEDIASTINUM, PLEURAL EFFUSION, ESOPHAGEAL PERFORATION, ASSOCIATED WITH FISH BONE IMPACTION: A CASE REPORT

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Background
Foreign body impaction and food bolus impaction is encountered commonly in clinical practice. In adults, fish bones and other bone fragments are the most commonly ingested foreign bodies with high risk perforation and iatrogenic perforation during extraction procedure. Once esophageal perforation develops, complications like cervical or mediastinal abscess, cervical or mediastinal emphysema (pneumomediastinum), pneumothorax, mediastinitis, or pleural effusion may also occur resulting respiratory failure.

Case presentation
A 68 years old woman was presented due to epigastric pain that penetrating up to the back right after having lunch one day before admission to hospital. Esophagogastroduodenoscopy showed corpus alienum (fish bone) near esophagogastric junction and a tear at esophagus wall. Extraction of corpus was done immediately and by the time corpus was extracted, the patient experienced worsening condition, developing respiratory failure due to pneumomediastinum, left pneumothorax and left pleural effusion. Patient was observed in intensive care, given symptomatic therapy including chest tube thoracotomy, and was discharged 23 days later.

Conclusion
Foreign bodies ingestion and extraction procedure may cause perforation with high morbidity, mortality and fatal complications such as pneumothorax, pneumomediastinum, and pleural effusion. Esophageal perforation and its complications should be quickly diagnosed, treated as early as possible and aggressively.

Keywords : *foreign body impaction, fish bone, pneumothorax, pneumomediastinum, pleural effusion, esophageal perforation*

POLYSACCHARIDE PEPTIDE (PSP) AS ASUPPORTIVE TREATMENT FOR MEDIASTINAL NEUROENDOCRINE TUMOR : A CASE REPORT

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Background

Mediastinal Neuroendocrine Tumor (NET) is a very rare type of mediastinal tumor, found in only <2% of all mediastinal tumor. Polysaccharide Peptide (PSP) extracted from medicinal mushroom Ganodermalucidum has been extensively researched and proven effective as adjuvant therapy for many types of cancer. We present a case of Mediastinal NET in which the patient showed significant clinical improvement after PSP was given as a part of supportive treatment.

Case Report

A 62 years old male, non-smoker, was referred to our hospital due to chronic cough and left lung nodule on chest radiograph. We took a Chest CT-Scan and found an Anterior Mediastinal Mass. The patient underwent midsternotomy and thetumor was removed completely, followed by adjuvant radiotherapy. Biopsy result revealed Mediastinal tumor carcinoid atypical predominant.The patient was symptomfree for 4 years. On January 2015, Chest CT Scan revealed a metastaticnodule in theupper left lung. The patient did not take chemotherapy due to low effectivity for this type of cancer. On September 2015, the patient was admitted to our hospital due to worsening condition. We decided to start giving PSP twice daily. The patient showed significant clinical improvement and got discharged. We followed up the patient for 3 years andobserveda slower disease progression and considerably good performance status.

Conclusion

Due to its negligible toxicity and many beneficial effects, polysaccharide peptide can become an option for supportive treatment in many cancer patients, including mediastinal NET.

Keywords: *Mediastinal Neuroendocrine Tumor, Mediastinal Carcinoid, Polysaccharide Peptide, Ganodermalucidum*

PRIMARY SPONTANEOUS PNEUMOTHORAX IN PREGNANCY WITH HYPEREMESIS GRAVIDARUM: A CASE REPORT AND LITERATURE REVIEW

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Background

Spontaneous Pneumothorax in pregnancy is a rare case. Hyperemesis Gravidarum is one of its risk factor.

Case

A case of 28 years old pregnant woman G5P3013 12-13 weeks in pregnancy with Hyperemesis Gravidarum was suffered from sudden onset of dyspnea and pleuritic chest pain. After clinical and supportive examination, patient was diagnosed by Primary Spontaneous Pneumothorax and observation was done. Significant improvement of symptoms recorded after two weeks of observation. Today, observation is still continued because high risk of recurrence in antepartum and intrapartum phase. Rupture of bleb or bulla subpleural after profuse vomiting was hypothesized as its pathology mechanism.

Conclusion

Pneumothorax is one of differential diagnosis in case of acute dyspnea and pleuritic chest pain in pregnant woman with HG. Definitive therapy, closed observation, and education are important to prevent pneumothorax complication in mother and child.

Keywords: *spontaneous pneumothorax, pregnancy, hyperemesis gravidarum*

RECURRENT PNEUMOTHORAX IN SJOGREN SYNDROME: A CASE REPORT

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Background and Aims

Pneumothorax is the presence of air in the pleural space between the lung and the chest wall. A patient who had a primary spontaneus pneumothorax is at risk of having a recurrence pneumothorax episode.[1] In Sjogren syndrome (SS), pneumothorax can be the first manifestation and recurrency can be happen. In 9–20% of cases, SS is associated with various respiratory symptoms and a female predominance.[2,3]

Case Report

A 35-year-old woman presented with acute dyspnea. She was previously diagnosed with SS in October 2017.On February 2018, she experienced pneumothorax two times and did not relieve after chest tube insertion so she referred to Respiratory Center Persahabatan Hospital. Her chest CT shows a left pneumothorax with multiple bullae and interseptal thickening lead to a suspection of lymphocytic interstitial pneumonia. The bronchoscopy showed no abnormality. *Video assisted thoracoscopic surgery* (VATS) and bullectomy were performed due to persistent air leaks. Histologically, there were alveol-emphysematous, focal lymphoid aggregates, infiltration of the peribronchiolar wall by lymphocytes with plasma cells and no cathamenial finding. *Interferon gamma release assay* (IGRA) test and Ca-125 marker were negative. Autoimmunity markers, including *antinuclear antibodies* (ANA) and *anti sjogren sindrome antigen A* (SS-A) antibody were positive. *Rheumatoid factor* (RF), anti *double stranded deoxyribonucleic acid* (ds-DNA) and *anti neutrophil cytoplasmic antibodies* (ANCA) were negative. The levels of C3 and C4 were within normal limits. There were no evidence of *human immunodeficiency virus* (HIV) and *human T-cell leukemia lymphoma virus* (HTLV) infection. *Acid fast bacilli* (AFB) examination and Gen Xpert from bronchial washing were negative.

Discussion

Recurrent pneumothorax as the first clinical symptom of SS has not been previously reported in Indonesia. In female, usually we assumed the cause of pneumothorax is cathamenial. We suspected the presence of an underlying immune disorder due to the findings on chest CT and histologically finding. According to the thoracoscopic findings in our case, pneumothorax was related to the rupture of subpleural bullae.[3]

Conclusions

Although rare, SS should be considered in Indonesian female patient presenting with recurrent pneumothorax.

THE COMPATIBILITY OF ANTIBIOTIC EMPIRICAL THERAPY ON PATIENTS WITH VENTILATOR ASSOCIATED PNEUMONI AT RSUP SANGLAH WITH ATS GUIDELINES 2005

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Background

Patient with VAP has mortality rate around 30% - 70%. An Adequate and Appropriate Antibiotic Empirical Therapy plays an important role in suppressing the mortality rate of VAP. RSUP Sanglah uses ATS Guidelines 2005 for treating VAP patients since it doesn't have its own guidelines yet.

Methods

To study the compatibility of antibiotic empirical therapy given in RSUP Sanglah with ATS Guidelines 2005 and also to determine other factors which influence the incompatibility this research use a cross sectional descriptive analytic design.

Material

Data collected from medical record of VAP patients in ICU at RSUP Sanglah.

Result

The result shows 70% of compatibility to 30% of incompatibility. The factors that mostly influence the incompatibility are comorbidities such as heart disease and metabolic disease thus lead to additional antibiotic therapy given outside of the guidelines.

Conclusion

Empirical Antibiotic Therapy for VAP at RSUP Sanglah is compatible with ATS Guidelines 2005 (70%), the other 30% of incompatibility is mostly influence by comorbidities on patient with VAP which result in additional type of antibiotic outside of the guidelines. Further studies must be done in RSUP Sanglah in order to make its own guidelines.

Keywords: *Ventilator Associated Pneumonia, antibiotic empirical therapy, ATS Guidelines 2005*

PREVALENCE AND RISK FACTORS OF REFLUX ESOPHAGITIS IN PATIENTS WITH STABLE COPD AT PERSAHABATAN HOSPITAL JAKARTA INDONESIA

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Background

Gastroesophageal reflux disease (GERD) is one of the most common causes of chronic cough and is a potential risk factor for exacerbation of chronic obstructive pulmonary disease (COPD), decreasing quality of life in COPD patients, aggravating symptoms both respiratory and gastro-intestinal. Forty patients were recruited consecutively from the outpatient of Asthma and COPD clinic at Persahabatan hospital Jakarta started from May 2017. The diagnosis of reflux esophagitis (RE) was based on the mucosal break on the esophageal lining through endoscopic examination. Exclusion criteria were COPD exacerbation and known esophageal disease.

Objectives

The aim of this study is to find the prevalence and risk factors of reflux esophagitis in stable chronic obstructive pulmonary disease (COPD) patients at persahabatan hospital Jakarta.

Methods

This is a cross sectional study among stable COPD patients who visited asthma-COPD clinics at Persahabatan Hospitalfrom July to November 2017. Forty patients were recruited consecutively started from May 2017. Interview, spirometry and endoscopy performed to all subjects who meet the inclusion criteria.

Results

A total forty subjects were enrolledin our study. Prevalence of RE in COPD was forty percent. There was no significant difference between the two groups regarding age, sex, used of ICS + LABA and BMI, although in the RE group has a slightly higher BMI. More severe airflow obstruction tends to increase in RE group although no significant statistical difference Most patients were elderly and smoker/ex. Exacerbation and CAT score were significantly associated with RE ($p<0.05$). Post BD spirometry showed greater airway and severe COPD tends to also had RE similar to results of other studies. Respiratory medication such as LABA, LAMA and SABA had an increased odds ratio (OR) to have RE. Heartburn as a symptom showed statistically significant to predict esophagitis ($p< 0.05$). COPD patients with RE had more symptoms and lower quality of life.

Conclusion

Prevalence of REwas high in COPD patient and even higher than previously reported in general patient with dyspepsia syndrome in Jakarta. Physician should consider RE as one of the most important comorbidities in COPD. Preventive strategy and clinical trials are warranted.

Keywords : COPD, Reflux esophagitis, exacerbation

SPIRATORY FAILURE REQUIRING EXTRACORPEAL MEMBRANE OXYGENGATION SECONDARY TO AUSTRIAN SYNDROME

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A 50 year old gentleman presented to the emergency department with new onset confusion and pyrexia. He had a 2 week history of right sided ear pain and coryza. He had no significant medical history, with high alcohol and cannabis intake. On clinical examination he had a GCS of 9, with no focal neurology, and normal cardio-respiratory and abdominal examination.

He was commenced on antibiotics and anti-virals for treatment of CNS infection. Cerebrospinal fluid analysis with polymerase chain reaction (PCR) was positive for streptococcus DNA. Due to agitation,he required ventilation and developed severe pneumonia. Despite antibiotic therapy he remained short of breath and developed pulmonary oedema, associated with a pan systolic murmur.

Echocardiography showed triple valve vegetations of the aortic, mitral and tricuspid valve. He developed respiratory failure secondary to severe streptococcal pneumonia, and heart failure secondary to triple valve endocarditis and required extracorpeal membrane oxygenation (ECMO).He required cardiac bypass surgery for aortic and mitral valve replacement and tricuspid valve repair. Mitral valve PCR was positive for streptococcal DNA. He made a full recovery and left hospital. This case presents streptococcal septicaemia associated with meningo-encephalitis, pneumonia and infective endocarditis. This rare triad, known as Austrian Syndrome, has previously been only been described in 34 cases in the literature, mainly seen in middle aged alcoholic men. This case highlights the key role in ECMO is respiratory failure, and how dissemination of streptococcal respiratory tract infection can affect multiple organ systems and cause significant morbidity.
Word Count: 244

Biography
Dr Mathew Vithayathil is an Academic Research Fellow working as part of the University of Cambridge and Addenbrooke's Hospital. He started his medical school undergraduate training at the University of Cambridge, achieving a 1st class honours degree in Physiology Development and Neuroscience, specialising in molecular pathways in phototransduction of Drosophila retina.

After this, Dr Vithayathil completed his medical clinical training at University College of London, achieving a degree with merit honours. He is currently training in general medicine and research, as part of the University of Cambridge Academic Research Fellowship. He has previously won research prizes, including the Royal Society of Medicine Herbert Reiss prize.

NON-INVASIVE VENTILATION (NIV) IN DESTROYED LUNG WITH HYPERCAPNIC RESPIRATORY FAILURE: A CASE REPORT

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Background
Destroyed lung is one of the lung condition that underlies respiratory failure.

Case presentation
A 54-year old women with history of complete tuberculosis (TB) treatment taken to National Respiratory Centre Persahabatan Hospital with dyspneu as chief complaint. Physical examination and radiological onfirmation concluded a destroyed lung.

Blood gas analysis was respiratory acidosis with hypercapnei far-above upper normal limit (59) while pO2 was low in 29,9.Her saturation was threatening: 47,3.

During hospitalisation, maximum effort for bronchodilation had been given: inhalation 6x/day,iv aminophylin and mucolytic drug.She showed improvement in saturation.However,pCO2 never reached normal with average of 78 (maximum was 104,5; pH 7,26).We assesed the patient as having respiratory failure (she once reached pH of within normal limit 7,357 while pCO2 70,8).We decided to apply a non-invasive ventilation (NIV) Optiflow and a significant improvement was shown very quick within one day into pCO2 58,4 from 83,1.This pCO2 change was followed by the better pH 7,38.After three days using NIV,we took off the NIV and adjusted her need of FiO2 with nasal canula.We have educated the patient for Long Term Oxygen Therapy (LTOT) to meet her lung condition.Unfortunetaly,within hours,the pCO2 risen again into 63,4 and she again experienced a drop in pH.

Conclusion
We saw a proof that in case of destroyed lung, hypercapnic condition can only be repaired temporarily by the NIV.

DOPPLER ECHOCARDIOGRAPHIC EVALUATION OF PULMONARY ARTERIAL HYPERTENSION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS

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Background

Chronic obstructive pulmonary disease (COPD) is an important cause of death and disability worldwide. It is expected to be the world 3rd and 5th leading cause of mortality and morbidity respectively in 2020. COPD is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation due to airway andor alveolar abnormalities usually caused by significant exposure to noxious particles or gases. Pulmonary arterial hypertension (PAH) is a common complication of COPD. Doppler echocardiography provides a rapid, noninvasive,and accurate method to evaluate the cardiac changes and early screening of patients with clinical suspicion of PAH.The aim of this study was to assess PAH secondary to COPD by doppler echocardiography.

Methods

Descriptive observational study was conducted at outpatient clinic of Dr Lukmonohadi Hospital Kudus, during January to March 2018. A total of35 patients with COPD were selected and staged by pulmonary function test and evaluatedby doppler echocardiography.PAH defined as an elevated mean pulmonary arterial pressure (mPAP) $\geq$ 25 mmHg.Estimation of mPAP using formula mPAP=79 – (0,45 x RVAcT).

Results

From the total of 35 patients with COPD, 20 (57.14%) weremen with mean age of 61.91 ± 11.08 years and the average body mass index of $20,81 \pm 5,08$ Kg/m2.On doppler echocardiographic evaluation, PAH was observed in 15 (42,86%) cases in which the prevalence of mild(mPAP 25-40 mmHg), moderate (mPAP 41-55 mmHg), and severe (mPAP > 55 mmHg) PAH were 5 (33,33%), 6 (40%), and 4 (26,67%), respectively. The frequencies of PAH in mild, moderate, severe, and very severe COPD were 23,08%, 41,67%, 62,5%, and 100%, respectively.

Conclusion

Prevalence of PAH has a relationship with severity of COPD. Echocardiography helps in early detection of cardiac complications in COPD cases giving time for early interventions.

Keywords: *Chronic obstructive pulmonary disease, pulmonary arterial hypertension, doppler echocardiography*

MASSIVE HEMOPTYSIS IN CHILDREN DUE TO INTRALOBAR PULMONARY SEQUESTRATION

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Background

Massive hemoptysis is defined as blood loss more than 200 ml per day, rare but potentially life threatening in children. Pulmonary sequestration (PS) is a rare congenital bronchopulmonary malformation accounting for 0.15% – 6.4% of all congenital pulmonary malformations, can be classified into intralobar sequestration (ILS) and extralobar sequestration (ELS). ILS is the most common type (75-85%). Main manifestations of PS are recurrent respiratory tract infection whereas hemoptysis is not a common symptom.

Case Report

Eight years old male child came to emergency department with massive hemoptysis (>400ml in 24 hours), with chest X-ray showing an opacity in the right lower lobe. This patient has a history of hemoptysis 10 months before and treated with antituberculosis drug but no improvement. We performed a flexible bronchoscopy, found an active bleeding from the right lower lobe and also multiloculated infiltration mass like polyp in right lower lobe and left lower lobe. CT angiography demostrated an intralobar pulmonary sequestration in the right and left lower lobes that provide arterial blood supply from thoracic aorta, vertebra artery and pulmonary artery.

Conclusion

We demonstrated a case of the lung sequestration in male children with chief complaint massive hemoptysis. Congenital pulmonary sequestration is a rare lung malformation. In cases of recurrent pulmonary infections of identical localization or recurrent hemoptysis, lung sequestration should be considered in children.The fact that using flexible bronchoscopy can find the source of bleeding and the abnormality of the airway.

ENDOTRACHEAL CHONDROID HAMARTOMA WITH MECHANICAL AIRWAY OBSTRUCTION : A CASE REPORT

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Background

Benign endotracheal tumor case are rare. The most common case of endotracheal tumor are malignant and only 10% being benign. Hamartoma was a benign tumor that made up of an abnormal mixture of cell and tissues founded in area of body growth. Hamartoma usually derived from primitive connective tissue such as cartilage, bone, fat, and smooth muscle. It is the most common benign tumor in the lung but rare in endotracheal.

Method and result

We are reporting a 24 years old male with chondroid hamartoma. The patient came to our hospital with distress of breath and stridor then he underwent a tumor extraction using rigid bronchoscopy with electrocauterization. Tumor removal was successes without any sequel of mechanical airway obstruction.

Conclusions

Endotracheal hamartoma was benign endotracheal tumor that rare occurs in airways.

Keywords : *benign endotracheal tumor, hamartoma, air way obstruction*

RESPIRATORY FAILURE, EFFECTS ON LENGTH OF STAY AND OUTCOMES: A HOSPITAL BASEDOBSERVATIONAL STUDY IN DR MOEWARDI HOSPITAL SURAKARTA

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INTRODUCTION

Respiratory failure is a common and major cause of illness and death. It is the main cause of death from pneumonia and chronic obstructive pulmonary disease (COPD), which together comprise the third-leading cause of death in the United States. It is also the main cause of death in many neuromuscular diseases. Epidemiologic studies suggest that respiratory failure will become more common as the population ages, increasing by as much as 80 percent in the next 20 years.[1-3]

Respiratory failure (RF) is defined as failure of oxygenation and/or carbon dioxide (CO_2) elimination. Hypoxemia occurs if arterial oxygen pressure (PaO_2) is below 60 millimeters of mercury (mmHg). Hypercapnia is present if arterial CO_2 pressure ($PaCO_2$) is above 50 mmHg. Hypoxemia and hypercapnia are frequently encountered in COPD patients with acute attack. The two types of acute and chronic respiratory failure are hypoxemic and hypercapnic. Acute respiratory failure (ARF) is a common and serious complication in hospitalized patients, may be caused by several conditions including pneumonia, chronic obstructive pulmonary disease (COPD), neurological disease and congestive heart failure (CHF).[2-4]

Respiratory failure patients may need Intensive care units (ICUs) care and its provide complex and expensive and hospitals face pressure to improve efficiency and reduce costs . Since costs are strongly related to ICU length of stay (LoS), shorter ICU LoS generally equates to lower costs.Patients LoS is associated with patient's severity of illness.[5]

Although hospital ventilator acquired pneumonia (VAP) infection and hopsital acquired pneumonia (HAP) infection in dr. Moewardi hosptial remains high 30.23 per mile and 2.41per mile respectively, below from the hospital strategic planning and target. This condition increase mortality,LoS and hosptal costs.[5]

In Indonesia, there is lack of study about the respiratory failure regarding patientscharacteristic and hospital performance.Central Java is one of the big provinces in Indonesia with the population of 34.674.870.This study was aim to analyze the effects of respiratory failureon length of stay and outcome ata teaching hospital in central java, indonesia.

MATERIAL AND METHOD

STUDY DESIGN

This is an observational analysis study of 110 patients, diagnosed as respiratory failure patients with arterial blood gas (ABG) pressurePO2 <60 mm Hg (7.8 kPa) or PCO2 >50 mm Hg (6.5 kPa) was conducted in Dr Moewardi Hospital, Surakarta from January 1, 2017 to December 31, 2017.

DATA COLLECTIONS

The patients were included in this study if they hadadmittted or consult with arterial blood gas (ABG) pressurePO2 <60 mm Hg (7.8 kPa) or PCO2 >50 mm Hg (6.5 kPa).
Data including gender, age, type of respiratory failure (TRF) which are hipoxemia and hypercapnia, length of

stay (LoS), the duration of respiratory failure(DRF) , onset of respiratory failure (ORF)   consist of acute and chronic and patients outcome were alive or death.

STATISTICAL ANALYSIS.
All the data were entered in MS Excel and analyzed in SPSS software (version 16.0). Univariate analysis was done to assess the distribution of baseline variables by computing frequency, percentages and mean with standard deviation. The data were described in table. Thereafter, chi-square test was used for analyzing difference in proportion for different variables. Spearman rank test was used for analyzing correlation in predictor effect of respiratory failure patients.   The data were confirmed as significant if P value obtained was <0.05.

RESULTS

1.   Patientcharacteristics

   Table 1.Respiratory failure patient characteristics

Characteristics	N	%
Gender		
Male	69	62.7
Female	41	37.3
Type of respiratory failure		
Hypoxaemia	85	77.3
Hypercapnia	25	22.7
Duration of respiratory failure		
Acute	95	86.4
Acute on chronic	15	13.6
Ventilator		
Yes	15	13.6
No	95	86.4
Intensive care		
Yes	27	24.5
No	83	75.5

Outcome

Alive	49	44.5
Dead	61	55.5

Primary diagnose

Asthma	2	1.8
Lung carcinoma	13	11.8
Oedem pulmonum	16	14.5
Lung micosis	2	1.8
PCP	2	1.8
Pneumonia	49	44.5
COPD	8	7.3
Tuberculosis	18	16.4

Table 2.Predictors characteristics

Variables	N	Minimum	Maximum	Mean	Std. Deviation
Age	110	21.00	92.00	55.03	15.36
Length of stay	110	1.00	28.00	8.80	4.65
Respiratory failure duration	110	1.00	12.00	5.27	2.78

A total of 150 patients of respiratory failure were collected from January, 1 2017 to December, 31 2017. Among those 150 respiratory failure patients69were male (62.7%), hipoxemia patients 85 (77.3%),acute respiratory failure 95 (86.4%) and 49 (44.5%) were diagnosed as pneumonia patients. Mean age of the patients was 55.03(±15.36) year old with length of stay 8.80 (±4.65), the duration of respiratory failure was 5.27 (±2.78).

2. **Resiratory failure effects and outcome of the patients**

Table 3.Respiratory failure patients outcome

variables	Alive		Death		P-value*
	N	%	N	%	
Ventilator					
Yes	9	8.2	6	5.5	0.309
No	40	36.4	55		

Intensive care unit

Yes		10	9.1	17	0.49
No		39	35.5	44	

*. Pearson Chi-Square

Respiratory failure patient frequency without ventilators died 55(50%), total 44(40.%) respiratory failure patients not admission at intensive care were died. Both were not statistical significant different.

3.   **Respiratory failure patients and correlation with predictors**

  Table 4.Respiratory failure patients correlation with LoS, DRF, TRF,ORF, age, and primary diagnose

variables		LoS	DRF	TRF	ORF	Age	Diagnose
LoS	r	1.000	.716**	-.049	-.179	-.196	.055
	P value	.	.000	.613	.061	.041	.569
DRF	r	.716	1.000	.021	-.077	-.048	.168
	P value	.000	.	.824	.421	.617	.078
TRF	r	-.049	.021	1.000	.417	.146	.176
	P value	.613	.824	.	.000	.128	.067
ORF	r	-.179	-.077	.417	1.000	.124	.150
	P value	.061	.421	.000	.	.195	.118
Age	r	-.196	-.048	.146	.124	1.000	.128
	P value	.041	.617	.128	.195	.	.181
Diagnose	r	.055	.168	.176	.150	.128	1.000
	P value	.569	.078	.067	.118	.181	.

**. Spearman correlation is significant at the 0.01 level (2-tailed).

*. Spearman correlation is significant at the 0.05 level (2-tailed).

The duration of respiratory failure correlated strongly and significantly with the length of hospital stay (P <0.001, R = 0.716). The patient's age correlated significantly with the length of hospital stay (P = 0.04). Onset of respiratory failure significant correlated withtype of respiratory failure (P <0.001)

DISCUSSION

The present study was conducted on 110 eligible patients with respiratory failure based on the ABG pressurePO$_2$ <60 mm Hg (7.8 kPa) or PCO2 >50 mm Hg (6.5 kPa). The baseline characteristics based on age, gender,type of respiratory failure, duration of respiratory failure, ventilator use, outcome, primary diagnose. The mean age was 55.03 with the range 21-92 years old, similar to a study in Turkey with age range was rather wide (21.0-98.0 years; mean age: 70.5±15.1 years).Male patients in this study was 69(69.7%) higher than female, the similar study show similar number in Taiwan with male patients was 68.9%. We found that the duration of respiratory failure correlated strongly and significantly with the length of hospital stay.[3, 6, 7]

Our findings in this study showed that only 15 (13.6%) patients with RF supported by mechanical ventilator, 95 patients were not supported and 50% among them was died. We found only 24.5 % patients with RF admitted in ICU and 86.4% were acute RF. These findings were diffrent to Unites State (US) where mechanical ventilator is the most commonly used supportive technique for acute RF in ICU.[8-10]

In our study, pneumonia was found 44.5 % from all RF patients lower than pneumonia cases in US 60% of all hypoxaemic ARF. Pneumonia is a significant cause of morbidity and mortality. Conceptually, pneumonia requiring admission to the ICU or carrying a high risk of death. Direct admission to an ICU is required for patients acute respiratory failure (ARF) requiring invasive mechanical ventilation. [3, 11, 12]

Our study further revealed that mean age of the RF patients was 55.03(±15.36) year old. Prior studies conducted in US showed the American RF patients was 67.1 (±16.4). This important data show younger critically ill adults patients with RF compared with US in our setting. Length of stay 8.80 (±4.65) day of the patients with RF in our hospital is high compared with Amsterdam study with mean 7.1 (±11.4) day. Although duration of ICU treatment (47 ± 39 days) or duration of mechanical ventilation (39 ± 38 days) were found in Germany for the patients with ARDS. The majorityof mechanically ventilated patients requireadmission to an intensive care unit(ICU), and the daily incremental cost ofmechanical ventilation for ICU patients isestimated at between $600 and $1500 perday in US. The duration of respiratory failure was 5.27 (±2.78) day in this study show the mean of improvement based on daily ABG follow up. Although in our study this findings were statistically not significant, the percentage of variables showed high proportion. [1, 8, 9, 13]

A remarkable finding in this study was the strong correlation found between the duration of respiratory failure with the length of hospital stay ($P <0.001$, $R = 0.716$). An interventional study in US showed length of hospital stay related with patients condition on RF.The small number of RF patients admitted the ICU correlated with hospital LoS. A study in Amsterdam found that the numbers of hospital or ICU beds increase ICU LoS decreases. The patient's age correlated significantly with the length of hospital stay is consistent with the emerging literature frommultiple studies showing that mortality rates among elderly RF patients age group were higher as found in patients older than 85 years in US 2009. Onset of respiratory failure significant correlated with type of respiratory failure ($P <0.001$) in this study, it relevant that hypoxemia and hypercapnia type correlated with acute and chronic condition based on natural disease of the RF patients. Taking into account the factor of acute and chronic RF might influence the outcomeof the patients.[4, 5, 11, 14, 15]

These findings have important implications,we suggest dr. Moewardi hospital, a teaching hospital and referral hospital for central java province as a study setting increase the numbers of hospital ICU beds. Correspond with the disease characteristic, this study also indicates the needs of respiratory high care unit

(RHCU) to allowed savings through the avoidance of an ICU admission and early treatment for RF patients. The limitation of our study weretherespiratory failurewe evaluate with various severity of disease and comorbidity factors that may also play a role in the outcome. Further study in grouping subjects with neuromuscular,heart failure and severity of disease is needed to determined the outcomes and effects of respiratory failure in the hospital.

CONCLUSION

Our study provides evidence of age, gender, ventilator use, ICU admission, diagnose, type of respiratory failure, length of stay were important variables in respiratory failure patients outcome. This will be pivotal for decision making regarding respiratory failure treatment.

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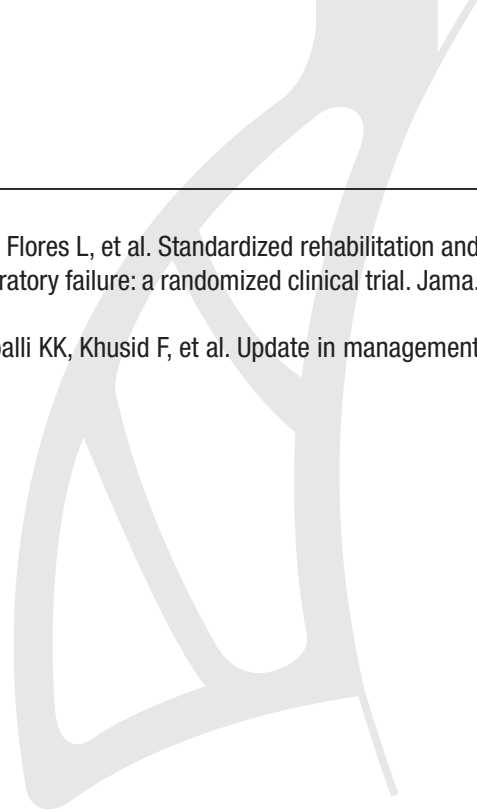
CHRONIC RESPIRATORY FAILURE IN UNILATERAL DIAPHRAGMATIC PARALYSIS WITH PNEUMONIA AND OBESITY PATIENT: A CASE REPORT

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Introduction

The diaphragm dysfunction may present as a partial impairment of the ability to create pressure (weakness) or the complete loss of diapragmatic function (paralysis). In the ICU setting, diaphragm dysfunction has recently grown to become a topic of significant interest because of its negative clinical impact on weaning outcome, length of mechanical ventilation, survival and long-term outcome.

Case Report

A 58 years old woman (BMI 42.2) presented at the Emergency Room with progressive dyspnea in the previous 12 hours. She also had cough with phlegm in 2 weeks. Physical examination existenced crackles in the both hemithorax. The blood gas analysis showed respiratory failure tipe 2. The chest X-Ray revealed a high dextra diaphragm, infiltrates in both lung, cardiomegaly. Patient was intubated and moved to Intensive Care Unit. She had a CT Thorax with the result : a high dextra diaphragm ec suspect paralysis of right phrenic nerve. She was being in ICU about 40 days and she had always depended on ventilator. After 2 weeks of her internsive care, she got bronchoscopy and trakeostomy with prolonged ventilator. When she was being observed without ventilator, she became dyspneu. Patient did a flouroscopy with the conclusion of a paradoxal right hemidiaphragm. She was consulted to a thorac surgeon and got a plan for a right diaphragm plication surgery.After surgery done, the patient can weaning from ventilator.

Discussion

Most patients with unilateral hemi-diaphragmatic weakness is asymptomatic. Several coexisting condition, such as obesity, underlying heart or lung disease, may worsen dyspnea.In our patient, coexisting condition are pneumonia and obesity. Most patient are usually detected incidentally on a routine chest X-Ray showing elevated hemidiaphragm. Patient did CT Thorax and floroscopy to confirm a diagnose.Because progression of the disease, tracheostomy with mechanical ventilation may be required.Surgical plication of the hemidiaphragm involves "tightening" the loose, paralyzed hemidiaphragm by oversewing its center. This therapy improved lung function and dyspnea in retrospective, uncontrolled trials.Our patient had consulted to a thorac surgeon and performed VATS plication surgery.

Conclusion

This case explained unilateral diaphragmatic paralysis caused chronic respiratory failure.

TUBERCULOUS MASTITIS DIAGNOSED ON CYTOLOGY – A RARE CASE REPORT

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ABSTRACT

Tuberculosis (TB) of the breast is an uncommon presentation of TB even in Indonesia where the incidence TB is high. TB of the mammary gland is a rare disorder often mistaken for other benign and malignant lesions of the breast. It occurs in females especially in their reproductive. Breast tuberculosis has no defined clinical features. Diagnosis is based on identification of typical histological features. Fine needle aspiration cytology (FNAC) is a very essential diagnostic tool in reaching to the conclusion.

A 31-year old multiparous nursing mother, with chief complaints a month history of lump, and pain in the left breast. On examination, there was a tender, ill-defined, irregular lump these measured 12x9x6cm, they were mobile and not attached to the overlying skin. There was left axillary lymphadenopathy. A provisional diagnosis of carcinoma of the left breast was made based on the clinical findings. A mammography showing high suspicion for malignancy. Her chest X-ray and complete blood was normal. Cytology, showed numerous lobular granulomas with central caseous necrosis surrounded by typical epithelioid macrophages and a thin rim of lymphocytes. There were a few Langhans type multinucleated giant cells in between the macrophages. She was commenced on a 6 month anti tuberculous therapy.

Cases of Tuberculous Mastitis (TM) can be diagnosed on FNAC when both epithelioid cell granulomas and necrosis are present. In tuberculosis-endemic countries, the finding of granuloma warrants empirical treatment for tuberculosis even in the absence of positive acid fast bacilli (AFB). This case shows that TM may present a diagnostic challenge on clinical, radiologic, and microbiological investigation. Indonesia where TB is endemic, we hope to generate awareness among physicians that a high index of suspicion should be expressed in evaluating breast masses and TB should be included in their differential diagnosis.

Key words: Tuberculosis (TB), Tuberculous mastitis, Fine needle aspiration cytology (FNAC)

PULMONARY REHABILITATION IMPROVE FUNCTIONAL CAPACITY AND QUALITY OF LIFE IN SEVERE COPD WITH COMORBIDITIES: A CASE REPORT

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Introduction

Patients with chronic obstructive pulmonary disease (COPD) typically manifest with worsening dyspnea, poor exercise tolerance and diminished quality of life. Comorbidities are commonly reported in COPD patients that significantly interfere progressive decline in physical activity and quality of life. Pulmonary rehabilitation (PR) is a comprehensive interventiondesigned to improve the physical and psychological condition of people with chronic respiratory disease to promote the long-term adherence to health-enhancing behaviors andalsoto reduce the negative impact of the comorbidities

Objective: To report the benefit ofPRin walking distance of the 6-min walk test (6MWT) and the St. George's Respiratory Questionnaire (SGRQ) score in severe COPD with comorbidities

Case Description

A 66 years old man with COPD grade D, bronchiectasis, congestive heart failure functional class II and controlled hypertention. He gets PR 3 timesweekly since 9 months ago, there are breathing exercise, endurance exercise, heating modality and upper extremity strengthening exercise but patient didn't routinely come to rehabilitation clinic. During that time, he had 2 times rehospitalization due to dyspneu cause by infected bronchiectasis and COPD exacerbation. Since january 2018 after his lastrehospitalization, patient has good compliance in PR.

The BORG scale 6-0-0, chest expansion 3-3-4 cm and diaphragm thickness in ultrasonography examination is 0,32 cm (normal range). After 12 weeks routinely PR, the walking distance of 6MWT improve 39 meters (MCID 25-30 m) and total SGRQ score decrease 3,87% especially in activity and impact domain

Conclusion:Pulmonary rehabilitation can improve functional capacity and quality of life in severe COPD withcomorbidities

Key words : pulmonary rehabilitation, COPD, comorbidities, functional capacity, 6MWT, quality of life, SGRQ

COMPARISON BETWEEN CLINICAL RISK SCORE (PSI, CURB-65, CRB-65) AND SERUM ROCALSITONIN IN ASSESSING PROGNOSIS (ICU ADMISSION, RESPIRATORY FAILURE, ORTALITY) OF COMMUNITY ACQUIRED PNEUMONIA IN BETHESDA HOSPITAL YOGYAKARTA

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Background

Community acquired pneumonia (CAP) is common among physicians and leads to hospitalization of a significant number of patients for death. Because of this, different specialty groups have tried to develop criteria or severity scoring systems. These scoring systems include PSI, CURB-65 and CRB-65. In addition, several inflammatory markers were identified with predictive capacity of the severity of pneumonia. Among the most widely studied biomarkers is serum procalsitonin (PCT). PCT are increasingly being used to distinguish bacterial pneumonia from other causes, to assess the prognosis of CAP and thereby aiming to complement severity scoring system.

Methods

A retrospective study was conducted of patients diagnosed with CAP. The subjects were 103 patients hospitalized between January 2017 to January 2018. To calculate the severity of pneumonia, patients were classified according to increasing serum PCT from baseline, PSI, CURB-65, and CRB. The ability to predict the final outcomes ICU admission, respiratory failure, and mortality were compared

Results

We studied 103 patients diagnosed with CAP (61 men and 42 women). The mean age of patients was 58,68 ± 19,28 years, 76.64% of all patients has comorbid diseases. PSI, CURB-65, CRB-65 and baseline serum PCT was measured, which was then stratified according to three categories of mild, moderate and severe risks. The ability to predicts ICU admission was almost same for PSI score and CURB-65 (AUC PSI 0.799 vs 0.794; $p < 0.001$), but higher than CRB-65 and PCT serum (AUC PSI 0.794 vs 0.719 vs 0.489; $p < 0.001$). The ability to predicts respiratory failure outcome was higher for PSI score compared to CURB-65, CRB-65, PCT serum (AUC PSI 0.827 vs 0.730 vs 0.760 vs 0.524; $p < 0.001$). The ability to predicts mortality was higher for PSI score compared to CURB-65, CRB-65, PCT serum (AUC PSI 0.923 vs 0.791 vs 0.781 vs 0.506; $p < 0.001$).

Conclusion

The management of severe CAP would be greatly improved if it were possible to identify the early of disease. Some of patients have comorbid factors who are most likely to develop complications and they are at risk of mortality. This study was aimed to assessing prognostic of CAP. PSI score and CURB-65 score have higher result than CRB-65 and PCT. To predict ICU admission, respiratory failure and mortality.

Key words: *CAP, predictive score, ICU, respiratory failure and mortality*

EFFECT OF PULMONARY REHABILITATION ON FUNCTIONAL CAPACITY IN STABLE COPD: IS DIFFERENT ABCD GROUP AFFECT THE OUTCOME?

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Introduction

There is evidence that pulmonary rehabilitation improves functional capacity in chronic obstructive pulmonary disease (COPD). In the refined assessment of COPD classification, ABCD groups are derived exclusively from symptoms and exacerbation history.

OBJECTIVE: To compare functional capacity change after pulmonary rehabilitation in stable COPD based on ABCD group classification.

Methods

This was retrospective cohort study. The subjects were patients with stable COPD group A to D who underwent pulmonary rehabilitation in Persahabatan Hospital, between July 2017 and May 2018. Their functional capacity was evaluated by 6-minute walking distance (6MWD) before and after receiving 2 months individually tailored pulmonary rehabilitation program. The 6MWD change among COPD groups was compared.

Results

Of the 13 subjects, the 6MWD was increase in 10(76.9%) subjects. The mean of 6MWD change after 2 months pulmonary rehabilitation was 79+85.84 m, which was statistically significant (p=0.025) and exceeds its minimum clinically important difference (25-35 cm). There was no significant difference in 6MWD change among different COPD groups (p=0.907).

Conclusion

The functional capacity of patient with stable COPD was significantly improved after 2 months pulmonary rehabilitation, but was not significantly different among groups. Pulmonary rehabilitation may improve functional capacity in all stable COPD regardless of the symptoms severity and exacerbation history.

Key words: pulmonary rehabilitation, COPD, ABCD group, 6MWD, functional capacity

EVALUATION OF PEAK COUGH FLOW, COPD ASSESSMENT TEST (CATTM) SCORE AND 6 MINUTE WALKING DISTANCE AFTER PULMONARY REHABILITATION IN PATIENT WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Introduction

Peak Cough Flow (PCF) measurement is an effective toolto measure cough ability. COPD patientshave inability to cough effectively,leads to symptoms that leads to decliningfunctional capacity . Assessment of symptoms for COPD patient is recommended using COPDAssessment Test (CATTM) score. The 6 Minute walk Test (6MWT) is a test that measure functional capacity of a patient.

Objective

To evaluate the effect of four weeks pulmonary rehabilitation on PCF measurement, CATTM score, and distance in 6MWTfor patients with COPD.

Materials and Methods

This is a historical cohort study. Physiatrist staff did the measurement for PCF, CATTM score and 6MWT of patient with COPD who underwent 4 weeks pulmonary rehabilitation program between Januay-June 2018.

Results

This study measure the PCF, CATTM score, and distance in 6MWT for 10 patients with COPD. PCF baseline value is 246 ± 57.19 L/ minute. At 1 month after intervention PCF value is 269 ± 70.78 ($p < 0.05$). CATTM baseline value is 13.1 ± 6.36 . At 1 month after intervention CATTM value is 15.2 ± 8.56 ($p > 0.05$). Distance in 6MWT baseline value is 296.4 ± 79.30 . At 1 month after intervention distance in 6MWT   is 339.3 ± 62.55 ($p > 0.05$).

Conclusion

Four weeks pulmonary rehabilitation program for COPD patient significantly improve PCF value but does not significantly improve CATTM score and distance in 6MWT .

Key words: Pulmonary Rehabilitation, COPD, PCF, CAT , 6MWT.

THE EFFECT OF INSPIRATORY MUSCLE STRENGTHENING EXERCISE WITH INSPIRATORY MUSCLE TRAINER AGAINST GAIT SPEED, USING A FOUR METER WALKING TEST IN CHRONIC OBSTRUCTIVE PULMONARY DISEASES (COPD) PATIENTS

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Background
Pathophysiology COPD is characterized by hyperinflation of the lung and resulting in decreased of the inspiration muscle strength. The present of dyspnea causes lowering down the gait speed. Currently, gait speed known as the sixth vital sign. The aim of this study was to know the relationship of inspiratory muscle strength with the gait speed.

Method
Thirteen patients with COPD assign in rehabilitation programs of Inspiratory Muscle Training for eight weeks. Data were performed every two weeks follow up basis. Patients trained at home for 30 minutes daily, minimum three days a week with 30% to 60% Maximal Inspiratory Pressure.

Results
There are an increase in respiratory muscle strength and gait speed with strong correlation($r = 0.6$) and statistically significant ($p < 0.05$).
Conclusion : Inspiratory muscle strengthening exercises with Inspiratory Muscle Trainer for 8 weeks can increase respiratory muscle strength and gait speed.

Key words: COPD, Inspiratory muscle trainer,gait speed, 4MWT, dyspnoe

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