SASM Society of Anesthesia and Sleep Medicine

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Pulmonary Hypertension and Sleep-Disordered Breathing/Obesity in the Perioperative Setting

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Disclosure

-Owner: SGM Consulting, LLC

-Co-Owner, COO: FC Monmouth, LLC, FC Monmouth Academy, LLC

-Consultant: Sandoz, Teikoku

-Patent: Multicatheter Infusion System. U.S. Patent No. US-2017-0361063

Objectives

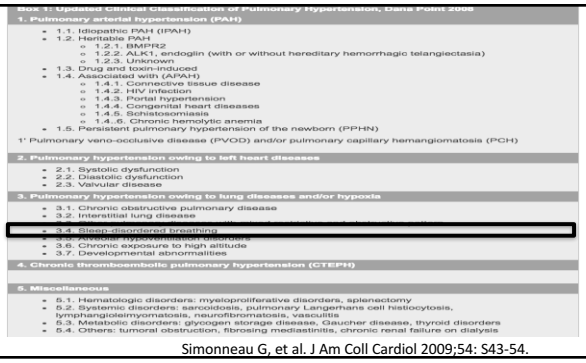
- Definition
- Epidemiology
- Perioperative Outcomes in Patients with PHTN
- Link Between OSA, Obesity and PHTN
- Effect of Surgery on PHTN
- Potential Efficacy of Disease Specific Interventions
- Conclusions

Definition and Classification

Definition

- PHTN = mean PAP at or above 25mmHG at rest or 30mmHG with exercise
  - Mild = 25-40mmHg
  - Moderate = 41-55mmHg
  - Severe = > 55mmHg

Badesch DB, et al. J Am Coll Cardiol 2009; 54:S55-66.



Box 1: Updated Clinical Classification of Pulmonary Hypertension, Dana Point 2008

1. Pulmonary arterial hypertension (PAH)

- 1.1. Idiopathic PAH (IPAH)
- 1.2. Heritable PAH
  - 1.2.1. BMPR2
  - 1.2.2. ALK1, endoglin (with or without hereditary hemorrhagic telangiectasia)
  - 1.2.3. Unknown
- 1.3. Drug and toxin-induced
- 1.4. Associated with (APAH)
  - 1.4.1. Connective tissue disease
  - 1.4.2. HIV infection
  - 1.4.3. Portal hypertension
  - 1.4.4. Congenital heart diseases
  - 1.4.5. Schistosomiasis
  - 1.4.6. Chronic hemolytic anemia
- 1.5. Persistent pulmonary hypertension of the newborn (PPHN)

1' Pulmonary veno-occlusive disease (PVOD) and/or pulmonary capillary hemangiomatosis (PCH)

2. Pulmonary hypertension owing to left heart diseases

- 2.1. Systolic dysfunction
- 2.2. Diastolic dysfunction
- 2.3. Valvular disease

3. Pulmonary hypertension owing to lung diseases and/or hypoxia

- 3.1. Chronic obstructive pulmonary disease
- 3.2. Interstitial lung disease
- 3.4. Sleep-disordered breathing
- 3.5. Alveolar hypoventilation disorders
- 3.6. Chronic exposure to high altitude
- 3.7. Developmental abnormalities

4. Chronic thromboembolic pulmonary hypertension (CTEPH)

5. Miscellaneous

- 5.1. Hematologic disorders: myeloproliferative disorders, splenectomy
- 5.2. Systemic disorders: sarcoidosis, pulmonary Langerhans cell histiocytosis, lymphangioleiomyomatosis, neurofibromatosis, vasculitis
- 5.3. Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
- 5.4. Others: tumoral obstruction, fibrosing mediastinitis, chronic renal failure on dialysis

Simonneau G, et al. J Am Coll Cardiol 2009;54: S43-54.

Epidemiology

The link between OSA, Obesity and PHTN

- Risk Factors include advanced age, OSA and obesity
- All very prevalent in orthopedic pts
- Prevalence
  - 6% of pts over 50 years
  - 5% of pts with BMI over 30kg/m2
  - 17-52% of OSA pts
  - Among those with PHTN 45% have OSA
  - Estimates suggest that 2.5Million pts with OSA have PHTN in US alone

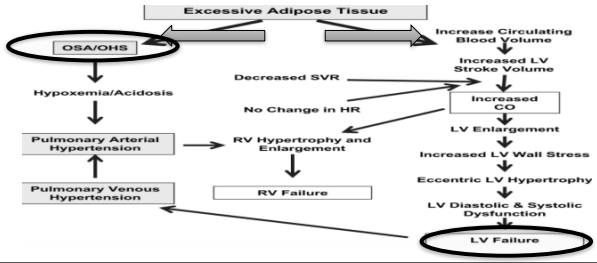
McQuillan BM, et al. Circulation 2001;104:2797–2802
Bady E, Thorax 2000;55:934–939
Krieger J, Chest 1989;96:729–737
Chaouat A, Chest 1996;109:380–386
Sajkov D et al. Am J Respir Crit Care Med 1999;159:1518–1526
Ulrich S, et al. Chest 2008;133:1375–1380

Pathophysiology

Role of Obesity in Cardiomyopathy and Pulmonary Hypertension

Clin Chest Med 30 (2009) 509–523

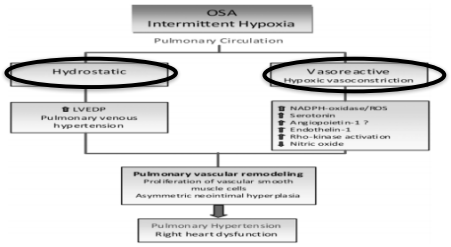
Charles S. Dela Cruz, MD, PhD, Richard A. Matthay, MD*



Pulmonary hypertension in obstructive sleep apnea: is it clinically significant? A critical analysis of the association and pathophysiology

Pulm Circ 2015;5(2):220-227.

Cyrus Kholdani, Wassim H. Fares, Vahid Mohsenin



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Vol. 47, No. 3, 2006
ISSN 0735-1097/06/$32.00
doi:10.1016/j.jacc.2005.11.015

Association of Subclinical Right Ventricular Dysfunction With Obesity

Chiew Y. Wong, MBBS, FRACP, Trisha O'Moore-Sullivan, MBBS, FRACP, Rodel Leano, BS, Craig Hukins, MBBS, FRACP, Carly Jenkins, BS, Thomas H. Marwick, MBBS, PhD, FACC

- TEE in N= 112 overweight or obese and referents (BMI <25 kg/m2), with or without OSA.
- RV systolic (s') and diastolic (e') velocities and strain indices

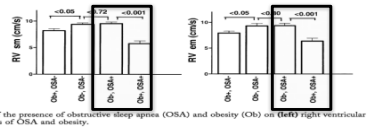


Figure 2. Differential effects of the presence of obstructive sleep apnea (OSA) and obesity (Ob) on **(left)** right ventricular (RV) s'_m and **(right)** RV e'_m in the four groups based on status of OSA and obesity.

Conclusions:
-Increasing BMI is associated with increasing severity of RV dysfunction in obese subjects, independent of sleep apnea.
-OSA decreases RV dysfunction in setting of obesity.

Sleep Breath
DOI 10.1007/s11325-011-0566-1

ORIGINAL ARTICLE

Mal-effects of obstructive sleep apnea on the heart

Song-qing Yang · Li-li Han · Xiao-lu Dong · Chun-yong Wang · Huan Xia · Pan Liu · Jing-hua Wang · Ping-ping He · Sheng-nan Liu · Ming-xian Li

Table 5 Changes of pulmonary artery systolic pressure in OSA patients

Group	Number of patients, *N*	Pulmonary artery systolic pressure (mmHg)
Control	35	22±5
Mild	33	28±6
Moderate	47	38±6*
Severe	41	55±11**

*$P<0.05$ (vs. mild); **$P<0.01$ (vs. moderate)

Frequency and Impact of Pulmonary Hypertension in Patients With Obstructive Sleep Apnea Syndrome

Omar A. Minai, MD[a,b,d,*], Basma Ricaurte, MD[a,b], Roop Kaw, MD[c], Jeff Hammel, MS[a,b], Mary Mansour, MD[c], Kevin McCarthy, RPSGT[a,b], Joseph A. Golish, MD[a,b,d], and James K. Stoller, MD[a,b]

Baseline characteristics

Characteristic	All (n = 83)	Pulmonary Hypertension		p Value*
		No (n = 25)	Yes (n = 58)	
Age (years)	56.7 ± 13	58.4 ± 13.6	55.9 ± 13	0.38
Gender				0.01
Men	48 (57.8%)	20 (42)	28 (58)	
Women	35 (42.2%)	5 (14)	30 (86)	
Body mass index (kg/m²)	34.3 ± 8.8	31.2 ± 6.9	35.6 ± 9.3	0.026
Hemoglobin (g/dl)	12.3 ± 1.9	12.3 ± 2.1	12.3 ± 1.9	0.76
Apnea-hypopnea index (events/hour of sleep)	30.8 ± 22.8	34.6 ± 27.8	29.1 ± 21.9	0.52
OSA severity by apnea-hypopnea index				0.42
Mild	39 (47%)	11 (28)	28 (72)	
Moderate	28 (34%)	7 (25)	21 (75)	
Severe	16 (19%)	7 (44)	9 (56)	
Nocturnal oxygen desaturation				0.13
<10% of total sleep time	48 (64%)	17 (35)	31 (65)	
≥10% of total sleep time	27 (36%)	5 (18)	22 (82)	
Not reported	8 (10%)	3 (37.5)	5 (62.5)	
Duration of nocturnal desaturation (% total sleep time)	16.7 ± 25.4	7.4 ± 12.1	20.5 ± 28.5	0.018
Mean pulmonary arterial pressure (mm Hg)	33.8 ± 13.6	18.7 ± 3.5	40.3 ± 11	<0.001
Cardiac index (Fick) (L/min/m²)	2.4 ± 1.1	2.65 ± 1.6	2.3 ± 0.9	0.16
Cardiac index <2	26 (35%)	4 (16%)	22 (38%)	0.09
Pulmonary vascular capacitance (ml/mm Hg)	3.0 ± 2.3	4.8 ± 2.9	2.2 ± 1.3	<0.001
Forced vital capacity(% predicted) (n = 51)	68.6 ± 16	75 ± 16	66.8 ± 16	0.042
Forced expiratory volume in 1 s (% predicted) (n = 51)	65.9 ± 17	70 ± 17	64.8 ± 16	0.31
Six-minute walk test (m) (n = 25)	295 ± 136	343 ± 213	285 ± 122	0.5

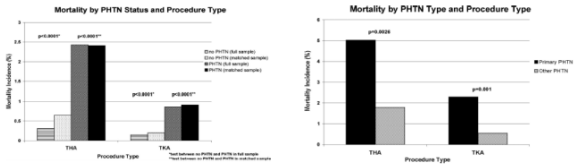
* p Value for comparison of patients with and without PH.

70% PTHN

Perioperative Outcomes

Perioperative Mortality in Patients with Pulmonary Hypertension Undergoing Major Joint Replacement

Stavros G. Memtsoudis, MD, PhD,* Yan Ma, PhD,† Ya Lin Chiu, MS,† J. Matthias Walz, MD,‡ Robert Voswinckel, MD,§ and Madhu Mazumdar, PhD†



Anesth Analg. 2010 Nov;111(5):1110-6.

Perioperative Outcomes after Unilateral and Bilateral Total Knee Arthroplasty

Stavros G. Memtsoudis, M.D., Ph.D., Yan Ma, Ph.D.,† Alejandro González Della Valle, M.D.,‡ Madhu Mazumdar, Ph.D.,§ Licia K. Gaber-Baylis, B.A.,‖ C. Ronald MacKenzie, M.D.,# Thomas P. Sculco, M.D.***

Table 5. Risk Factors for Perioperative Mortality after Total Knee Arthroplasty—Comorbidities (Model 2)

Comorbidity	Regression Coefficient Estimate	Odds Ratio	95% CI	*P* Value
Alcohol abuse	0.25	1.28	0.57–2.88	0.552
Chronic lung disease	0.18	1.2	0.98–1.47	0.0844
Congestive heart failure*	1.62	5.03	4.14–6.11	< 0.0001
Uncomplicated diabetes mellitus	0.12	1.13	0.92–1.39	0.2475
Complicated diabetes mellitus	0.13	1.13	0.67–1.92	0.643
Liver dysfunction	0.28	1.32	0.55–3.17	0.5381
Coagulopathy*	0.96	2.62	1.8	
Neurologic disorders*	1.03	2.8	1.0	
Obesity	−0.26	0.77	0.5	
Peripheral vascular disease*	0.4	1.5	1.0	
Renal disease*	1.25	3.49	2.5	
Pulmonary circulatory disease*	2.46	11.75	9.05–15.25	< 0.0001
Cardiac valvular disorders	0.12	1.12	0.84–1.49	0.4278
Electrolyte/fluid abnormalities*	1.3	3.67	3.06–4.4	< 0.0001
Metastatic cancer*	1.33	3.76	1.09–13.02	0.0364
Cancer	0.18	1.2	0.54–2.68	0.6535

NIS
3.4 Million patients 1998-2006

Pulmonary circulatory disease* 2.46 11.75 9.05–15.25 < 0.0001

Anesthesiology 2009; 111:1206–16

Perioperative Insults Worsening PHTN

Perioperative Insults Worsening PHTN

- Hypoxemia
- Hypercapnia (hypoventilation, CO2 peritoneum)
- Acidosis
- Hypothermia
- Hypervolemia
- Increase in intrathoracic pressure (mechanical ventilation/pneumoperitoneum)
- Insufficient anesthesia and analgesia/sympathetic surges

PHTN in Orthopedic Patients Pathophysiology

Orthopedic Pathophysiology

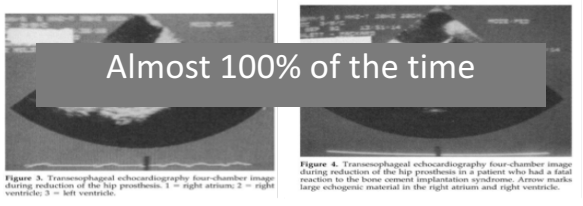


Figure 3. Transesophageal echocardiography four-chamber image during reduction of the hip prosthesis. 1 = right atrium; 2 = right ventricle; 3 = left ventricle.

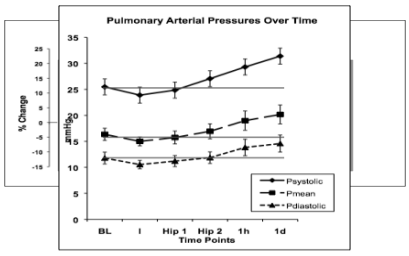
Figure 4. Transesophageal echocardiography four-chamber image during reduction of the hip prosthesis in a patient who had a fatal reaction to the bone cement implantation syndrome. Arrow marks large echogenic material in the right atrium and right ventricle.

Almost 100% of the time

Urban et al, Anesth Analg 1996; 82:1225-9

Perioperative Pulmonary Circulatory Changes During Bilateral Total Hip Arthroplasty Under Regional Anesthesia

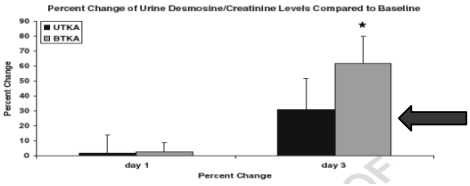
Stavros G. Memtsoudis, MD, PhD, FCCP, Eduardo A. Salvati, MD,† George Go, BS,* Yan Ma, PhD,‡ and Nigel E. Sharrock, BMedSci, MB, ChB**



Reg Anesth Pain Med. 2010 ;35:417-21.

Urine Desmosine as a Marker of Lung Injury Following Total Knee Arthroplasty. A Pilot Study

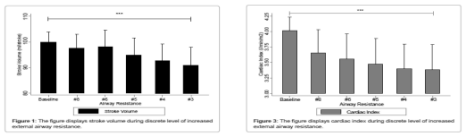
Stavros G. Memtsoudis, MD, PhD · Barry Starcher, PhD · Alejandro González Della Valle, MD · Yan Ma, PhD · Kethy Jules-Elysee, MD · Thomas P. Sculco, MD



Memtsoudis et al., HSS J 2009 ;5:154-8

Hemodynamic Response to Dynamic Changes in Upper Airway Impedance – A Volunteer Study

Ottokar Stundner[1,2], Thomas Danninger[2], Isabelle Kao[2], Peter Gerner[2] and Stavros G Memtsoudis[3*]



J Anesth Clin Res 2013, 4:5

So what do I do?

Difficulty diagnosing

- "Double occult disease" – majority of OSA patients is undiagnosed at time of surgery
- and PHTN is an occult disease
- Technically difficult to do echo in obese patients
- Ortho patients often physically not able to tolerate exercise, i.e. 6 min walk test.

European Heart Journal (2009) **30**, 2493–2537
doi:10.1093/eurheart/ehp297

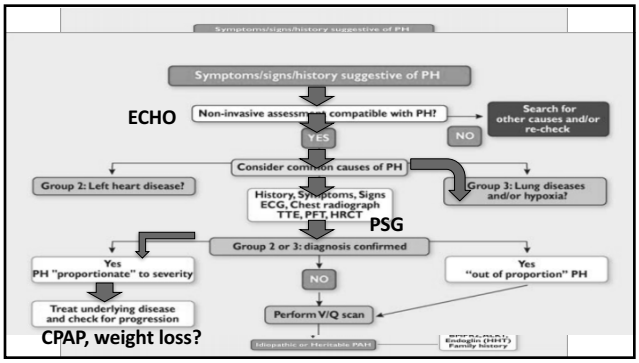
ESC/ERS GUIDELINES

Guidelines for the diagnosis and treatment of pulmonary hypertension

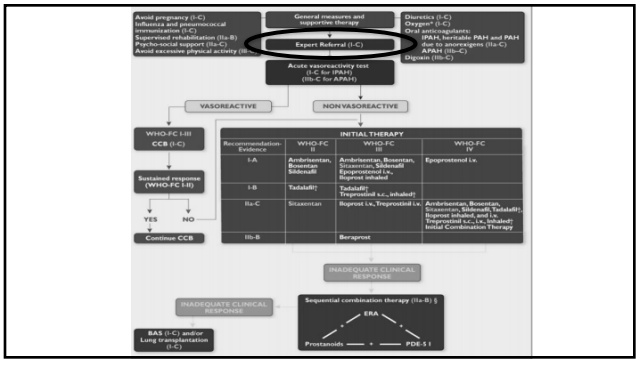
The Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS), endorsed by the International Society of Heart and Lung Transplantation (ISHLT)

Table 3: Clinical findings in patients with pulmonary hypertension (mod. [8]).

(i) Dyspnea (during stress/at rest)/cyanosis
(ii) Fatigue
(iii) Dizziness
(iv) Syncope
(v) Thoracic pain
(vi) Palpitations
(vii) Orthopnea
(viii) Cough
(ix) Croakiness
(x) Abdominal tension
(xi) Peripheral Edema/Ascites
(xii) Hepatomegaly



Preoperative Treatment



Impact of Disease Specific Interventions on PHTN in OSA and Obese Patients

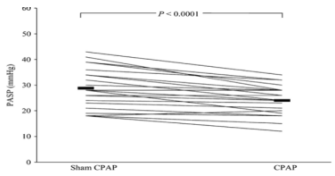
European Heart Journal (2006) 27, 1106–1113
doi:10.1093/eurheartj/ehl007

Clinical research
Hypertension

Pulmonary hypertension in obstructive sleep apnoea: effects of continuous positive airway pressure
A randomized, controlled cross-over study

Miguel A. Arias[1], Francisco García-Río[2*], Alberto Alonso-Fernández[2], Isabel Martínez[2], and José Villamor[2]

- N=23 OSA patients, 10 PHTN
- 3 months CPAP



Respiration

Clinical Investigations

Daytime Pulmonary Hypertension in Patients with Obstructive Sleep Apnea

The Effect of Continuous Positive Airway Pressure on Pulmonary Hemodynamics

Alchanatis M.[a] · Tourkohoriti G.[a] · Kakouros S.[b] · Kosmas E.[a] · Pedaras S.[a] · Jordanoglou J.B.[a]

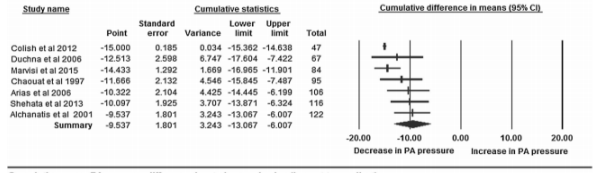
- N=29
- 20% with OSA had PHTN that was clinically mild (mean PAP, 25.6 mm Hg).
- PHTN pts were older and increased BMI
- 6 months of CPAP treatment was associated with reductions in mean PAP in OSA pts with PHTN (25.6 ± 4.0 to 19.5 ± 1.5 mm Hg) and those without PHTN (14.9 ± 2.2 to 11.5 ± 2.0 mm Hg).

Alchanatis M, et al Respiration 2001;68:566–572.

Heart Fail Rev (2016) 21:591–598
DOI 10.1007/s10741-016-9548-5

Effect of continuous positive airway pressure treatment on pulmonary artery pressure in patients with isolated obstructive sleep apnea: a meta-analysis

Tasnim F. Imran[1] · Marya Ghazipura[2] · Spencer Liu[2] · Tanzib Hossain[3] · Hormoz Ashtyani[4] · Bernard Kim[4] · J. Michael Gaziano[1] · Luc Djousse[1]



Cumulative mean PA pressure difference by study sample size (largest to smallest)

Obesity Surgery, *14*, 755-762

Effect of Bariatric Surgery on Obstructive Sleep Apnea and Hypopnea Syndrome, Electrocardiogram, and Pulmonary Arterial Pressure

Matilde Valencia-Flores, PhD[1,5]; Arturo Orea, MD[2]; Miguel Herrera, MD, PhD[3]; Victoria Santiago, MS[1]; Verónica Rebollar, MD[2]; Violeta A. Castaño, MS[1]; Jorge Oseguera, MD[2]; Jorge Pedroza, MD[4]; Jorge Sumano, MS[1]; Montserrat Resendiz, MS[1]; Guillermo García-Ramos, MD[1]

Pulmonary Artery Pressure

Before surgery, 28 patients (96.5%) presented pulmonary arterial hypertension (range 31.0-80.5 mmHg). After surgery, it completely resolved in only 4 patients. However, mean SPAP significantly decreased in the group of obese patients in whom OSAHS resolved after surgery from a mean of 61.4±15.8 mmHg to a mean of 42.6±9.2 mmHg. In

Anesthetic Care

European Heart Journal (2009) 30, 2493–2537
doi:10.1093/eurheartj/ehp297

ESC/ERS GUIDELINES

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The Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS), endorsed by the International Society of Heart and Lung Transplantation (ISHLT)

It is recommended to avoid pregnancy in patients with PAH	I	C
Immunization of PAH patients against influenza and pneumococcal infection is recommended	I	C
Physically deconditioned PAH patients should be considered for supervised exercise rehabilitation	IIa	B
Psychosocial support should be considered in patients with PAH	IIa	C
In-flight O_2 administration should be considered for patients in WHO-FC III and IV and those with arterial blood O_2 pressure consistently [illegible]	IIa	C
Epidural anaesthesia instead of general anaesthesia should be utilised, if possible, for elective [illegible]	IIa	C
Excessive physical activity that leads to distressing symptoms is not recommended in patients with PAH	III	C

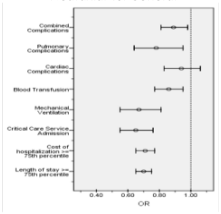
*Class of recommendation.
†Level of evidence.

Sleep Apnea and Total Joint Arthroplasty under Various Types of Anesthesia

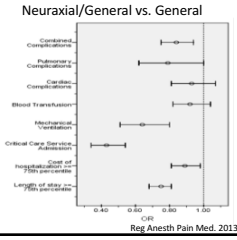
A Population-Based Study of Perioperative Outcomes

Stavros G. Memtsoudis, MD, PhD, FCCP, Ottokar Stundner, MD,* Rehana Rasul, MPH,† Xuming Sun, MS,† Ya-Lin Chiu, MS,† Peter Fleischut, MD,‡ Thomas Danninger, MD,* and Madhu Mazumdar, PhD†*

Neuraxial vs. General



Neuraxial/General vs. General



Reg Anesth Pain Med. 2013;38:274-81.

Hindawi Publishing Corporation
Anesthesiology Research and Practice
Volume 2012, Article ID 356982, 16 pages
doi:10.1155/2012/356982

Review Article

Perioperative Anesthesiological Management of Patients with Pulmonary Hypertension

Jochen Gille,[1] Hans-Jürgen Seyfarth,[2] Stefan Gerlach,[1] Michael Malcharek,[1] Ilke Czeslick,[3] and Armin Sablotzki[1]

Table 9: Authors recommendations for the human and structural and technical requirements for the perioperative management of patients with severe pulmonary hypertension.

(i) Established cooperation with cardiologists and pulmonologists
(ii) Access to specific medication for the treatment of pulmonary hypertension
(iii) Experiences in all procedures of general and regional anesthesia
(iv) Experiences in dealing with pulmonary arterial catheterization and the use of inhaled drugs for selective pulmonary vasodilation
(v) Intraoperative transesophageal echocardiography
(vi) Hemodynamic monitoring in critical care
(vii) Specific educational program for "pulmonary hypertension"
(viii) Consultants with special experiences in the treatment of pulmonary hypertension
(ix) Regular pain visits and/or pain nurses for the perioperative pain therapy

Summary

- PHTN is common in patients with OSA and obesity.
- The underlying pathophysiology of each disease process maybe synergistic and potentially additive in the development of PHTN.
- A high level of suspicion is needed for diagnosis and referral to expert care is advised.
- PHTN is associated with adverse perioperative outcomes.
- PHTN can worsen perioperatively due to a number of mechanisms.
- The treatment of obesity and OSA may reduce the severity of PHTN and potentially cure it.