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Case Report: Anesthetic Management in Pregnant Woman with Severe Pulmonary Hypertension

Mariana Ortega Martínez[1], Karla Iveth Cabildo Clemente[2], Fernando Alberto Avelar Ocampo[3]

[1]Third year resident physician of anesthesiology. General Hospital of Cancun. Faculty of Medicine of the Autonomous University of Yucatan.

[2]Anesthesiologist assigned to the anesthesiology service, Cancun General Hospital.

[3]Third year resident physician of anesthesiology. General Hospital of Cancun. Faculty of Medicine of the Autonomous University of Yucatan.

ABSTRACT

Pulmonary hypertension is a disease of low prevalence that can affect women of childbearing age; however, it is the cardiovascular disease with the highest maternal mortality, up to 56%. Timely counseling and optimization of care during pregnancy and the peripartum period have reduced maternal mortality. We present the case of a 41-year-old female patient with a history of unspecified heart disease of 10 years of evolution without medical treatment and congenital hypoplasia of the right thoracic limb. She came to the emergency department with pregnancy of 22.3 weeks of gestation, dyspnea of medium efforts, peribuccal cyanosis and pulmonary murmur, so a transthoracic echocardiogram was performed at rest that reported moderate tricuspid insufficiency/mild aortic insufficiency/moderate pulmonary insufficiency with high probability of pulmonary hypertension, so it was suggested to interrupt the pregnancy via abdominal, which was denied by the patient and a referral to third level of care was made. Patient was readmitted at 34 weeks of gestation with dyspnea on small efforts and labor in latent phase, so an emergency cesarean section was performed, with anesthetic management with fractionated peridural block, leaving the room with spontaneous ventilation, without vasopressor support to ICU, which later presented a torpid evolution until death.

KEYWORDS: maternal mortality, pulmonary hypertension, pregnancy, heart disease, anesthesia management

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INTRODUCTION

Pulmonary hypertension is defined as a mean pulmonary arterial pressure >25 mmHg at rest, estimated by right heart catheterization.(1) The causes of this disease are multifactorial; they have been classified into five groups, highlighting: pulmonary arterial hypertension proper, pulmonary hypertension associated with left heart disease, pulmonary hypertension associated with lung disease, pulmonary hypertension associated with thromboembolic disease, and miscellaneous causes. The most common is left heart disease (up to 78.3%), the most serious complication of which is Eisenmenger's syndrome.(2)

Pulmonary artery hypertension is characterized by diffuse obstruction and obliteration of the pulmonary arteries, which leads to increased resistance to blood flow to the lungs, causing the right ventricle to try to compensate by generating higher pressure to maintain pulmonary blood flow.(3) When the right ventricle cannot achieve this due to increased resistance, progressive heart failure develops and eventually death. In all cases, the presence of progressive dyspnea, syncope and angina should be investigated.(4)

There are three moments of special risk of decompensation during pregnancy, which must be faced with special caution: 1) At the end of the second trimester due to the greater expansion of plasma volume, 2) During labor, uterine contractions produce increased cardiac output by a compressive mechanical effect, 3) Immediate Puerperium, delivery and uterine retraction, releases the mechanical obstruction of the vena cava with increased venous return.(4,5)

Heart disease is associated with a morbidity and mortality rate of 30 to 56%, with the immediate puerperium being the period of greatest risk, and fetal mortality can reach 28%.[6,7] Medical attention aimed at controlling pulmonary hypertension during pregnancy significantly reduces the associated complications and increases the possibility of obtaining a healthy newborn.[8,9]

CLINICAL CASE

Female patient, 41 years old, with a history of heart disease unstudied for 10 years, no medical diagnosis or treatment, congenital malformation of the right thoracic limb and short stature. Menarche 14 years, IVSA 14 years, regular 30x5 cycles, MPF: none, G1.

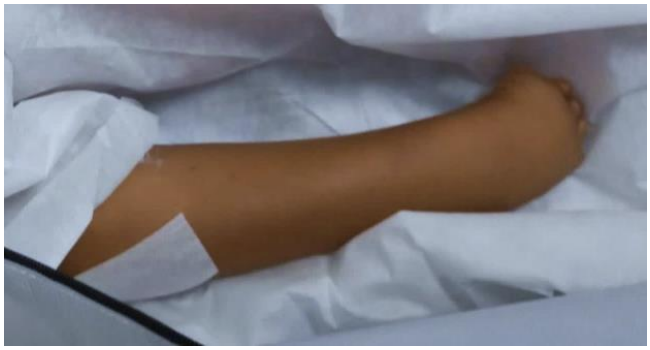

Figure 1. Upper limb malformation: Absence of forearm and finger hypoplasia.

She came to the emergency department reporting mild dyspnea when performing daily activities, with SaO2 96%, physical examination with pallor of the integuments, scarce peribuccal cyanosis, jugular ingurgitation grade I, unspecified pulmonary murmur, hypoplastic right thoracic limb, capillary filling 3 seconds, edema of extremities +, so an admission diagnosis of Pregnancy of 22.3 weeks of gestation by USG of second trimester + unspecified heart disease was integrated. A transthoracic echocardiogram was performed at rest with LVEF 50%, dilated right ventricle with pressure and volume overload, moderate tricuspid insufficiency, mild aortic insufficiency, moderate pulmonary insufficiency with dilation of the pulmonary artery with high probability of pulmonary hypertension, with a PSAP 95.5 mmHg and TAPSE 20.2 mm. She is evaluated by the Gynecology service, which suggests hospitalization to end her pregnancy for maternal benefit, however, it is denied. She is also evaluated by the Cardiology service who mentions that she does not deserve medical treatment and refers her to the 3rd level of care.

In her second emergency visit, patient came two months later with exacerbation of dyspnea with 92% SaO2, paraclinical tests were performed highlighting thrombocytopenia of 113/mm3, Obstetric USG was performed with report of pregnancy 25.5 sdg, weight 845 grams, with simple circular cord, ECG with pulmonary P wave in DII and AVF, and inversion of T wave in V1 and V2. Toxemic profile was requested, which was not pathological. Patient reported not to refer to the third level, so hospital admission was insisted, without success, with voluntary discharge signature.

The patient came to her third consultation with obstetric pain of 3 days of evolution, accompanied by dyspnea on small efforts, asthenia, adynamia, referring fetal movements, with SaO2 48%, HR 112 bpm, peripheral cyanosis, FHR 118 bpm, cervix 2 cm dilated, 40% effacement, amnion intact, edema of the lower limbs ++, delayed capillary filling. Paraclinical tests were performed again with glucose 136 mg/dl, urea 25 mg/dl, uric acid 12.9, BUN 8.8 mg/dl, creatinine 0.5 mg/dl, hb 11.9 g/dl, ht 36.3%, leukocytes 6.4, platelets 129,000, PT 11.8, PTT 28.8, INR 1.03, fibrinogen 93, evaluation by the Cardiology service was requested, who recommended interruption of pregnancy due to exacerbation of heart disease.

Admitted to the operating room with a diagnosis of Pregnancy 34 weeks of gestation due to LMP/unspecified cardiomyopathy with severe pulmonary hypertension/TPFL/mild thrombocytopenia/satisfied parity, for cesarean section + BTL. Patient is admitted to the ward, type 1 monitoring is performed, with the following vital signs on admission: BP 115/64 mmHg, HR 101 bpm, SatO2 52% with mask with reservoir, no oxygen, stuporous, generalized pallor of the integuments, peripheral cyanosis, hypoventilated lung fields, lower limb edema ++.

Supplemental oxygen is administered with a mask with reservoir with FiO2 at 70% and anesthetic technique is performed with fractionated peridural block in left lateral decubitus with Lidocaine 2% 140 mg PD + Fentanyl 150 mcg PD, functional peridural catheter is introduced, latency of 15 minutes is given, reaching T5 diffusion, without toxicity data, with vital signs after anesthesia: BP 121/71, HR 99, SaO2 77%. The patient was placed in supine decubitus, without tolerating the position, so the surgical procedure was performed in a semi-fowler position.

A live product was obtained, female, with simple circular cord, born in apnea, hypotonic, HR 60 bpm, so 1 cycle of 15 seconds PPV was started, with partial improvement, so advanced airway management was decided, weight 1730 grams, height 43 cm, Capurro not assessable, Apgar 6/8, Silverman not assessable, with meconium + fluid.

It was decided to use Carbetocin 50 mcg IV bolus as uterotonic, obtaining an adequate uterine tone. The surgical-anesthetic procedure was concluded and the patient was discharged to intensive care with spontaneous ventilation, with a mask with a 70% FiO2 reservoir, without vasopressor support, with the following vital signs at discharge: BP 120/71 mmHg, HR 101 bpm, SaO2 63%. Peridural catheter was left in place until clinical and paraclinical reevaluation.

Subsequently, she was admitted to the ICU with the following vital signs: BP 132/70 mmHg, HR 101 bpm, RR 20 rpm, SaO2 63%, MAP 86, with face mask with reservoir with FiO2 at 70%. Four hours after admission, the patient presented transvaginal bleeding of 300 cc, so she was evaluated by Gynecology, who commented that it was compatible with

lochia, misoprostol 800 mcg rectally was indicated, with partial cessation of bleeding, during the night the patient presented increased transvaginal bleeding with exacerbation of dyspnea with supplemental oxygen with CPAP with FiO2 at 100% with SaO2 20%, Therefore, advanced airway management was decided with rapid intubation sequence, direct laryngoscopy was performed at the first attempt, Cormack 2 and she was coupled to volume-controlled IMV, FiO2 at 100%, PEEP 10, FR 20, VT 300, with MAP 68. New paraclinics are performed with TB 2.8, DB 1.8, IB 1, TGO 2793, TGP 1215, dimer D 3155 ng/dl, glucose 58, urea 77.9, BUN 36, creatinine 2.4, uric ac 14.9, Cl 106, Na 138, K 6. 2, Hb 13.3, hto 41, leukocytes 28.7, neu 86.9, platelets 8,000, urine proteins 300 mg/dl, arterial blood gas with pH 6.9, pco2 32, hco3 7.9, lactate 10, BE -23, PO2/FIO2 45, GAP anion 23. Patient evolves torpidly and one day after admission to ICU, he requires double vasopressor with norepinephrine - vasopressin and double inotropic with dopamine - dobutamine. The patient presented data of multiple organ failure, so antikalemic measures with calcium gluconate, diuretic, MNB with salbutamol and platelet transfusion were indicated.

Cardiology evaluation was requested and a transthoracic echocardiogram was performed with report of right heart failure secondary to dilatation of right chambers and with data of severe pulmonary hypertension, moderate pulmonary insufficiency, severe tricuspid insufficiency, mild aortic insufficiency.

Patient died with a diagnosis of refractory cardiogenic shock/multiple organ failure/unspecified heart disease/severe pulmonary hypertension/immediate pathological perioperative period.

The newborn was evaluated by the pediatric cardiology service, with an echocardiogram that reported transverse aortic arch and borderline isthmus without hemodynamic repercussions, patent foramen ovale with left to right shunt, with pulmonary pressure in normal ranges, with preserved biventricular systolic and diastolic function. The newborn was discharged hemodynamically stable, with spontaneous ventilation, with an outpatient appointment for follow-up by the Pediatric Cardiology service.

DISCUSSION

Pulmonary hypertension (PH) is estimated to affect 1.1 out of every 100,000 pregnancies, generating a high maternal mortality which is close to 50%, however, with adequate treatment, mortality can be reduced by 15 to 30%.[10,11]

The main recommendation of international guidelines on the management of patients with PH in pregnancy is to offer termination of pregnancy.[12] However, it is important to recognize the key points of management in patients who wish to continue with pregnancy, in these cases the available therapeutic approach should be taken into account.[13]

In our clinical case, it was not possible to perform a pre-anesthetic evaluation, however, the congenital defect in the right upper extremity and the heart disease present are striking, so it is thought that it may be related to Holt-Oram syndrome.

Holt-Oram syndrome is an autosomal dominantly inherited disorder with 100% penetrance, the causative gene TBX5 on chromosome 12 was discovered in 1997 and has an estimated incidence of 1/100,000 live births.[14] Clinically it associates skeletal abnormalities of the upper extremity in 100% with cardiovascular abnormalities in 75%.[15] It can present as an isolated or familial form, clinical manifestations vary from hypoplasia of the thumb to partial or complete agenesis of the upper limbs.[16] It is a rare disorder with an estimated incidence of 1/100,000 live births.

From the cardiac point of view, the most frequent malformation is atrial septal defect, although the possibility of ventricular septal defect, mitral valve prolapse, hypoplastic left hemicardium, dilated cardiomyopathy and arrhythmias of various types has been described.[17] In the present clinical case, there is no specific structural evidence of any heart disease in the echocardiogram, so it is thought to be pulmonary hypertension associated with connective tissue diseases, it is considered prudent to perform a rheumatologic and genetic profile of her daughter to rule out a specific cause.

Guido MM, et al. conducted a study of 900 patients with severe aortic stenosis undergoing TAVI with echocardiographic analysis prior to the procedure, where the right ventricle-pulmonary artery (RV-PA) relationship, defined as the capacity of the RV to handle afterload, was evaluated and can be estimated by measuring the ratio between tricuspid annular plane systolic excursion (TAPSE) and pulmonary artery systolic pressure (PSAP) by echocardiography. A TAPSE/PSAP < 0.32 mm/mmHg (sensitivity: 87.5% and specificity: 75.9%) identifies severe abnormal RV-PA coupling, and this has been shown to be a strong independent predictor of long-term mortality.[18]

During the first consultation in the emergency department, the patient reported symptoms compatible with CHF with NYHA functional classification II and WHO classification class IV, also with signs of hypoperfusion and systemic congestion, with a TAPSE/PSAP ratio of 0. 21 mm/mmHg, with a high predictive value for mortality, and therefore, as she wanted to continue with pregnancy, medical treatment based on prostaglandin analogues, selective phosphodiesterase 5 inhibitor or calcium antagonists should be started and an adequate multidisciplinary follow-up should be carried out to regulate behavior.

The goals of anesthetic management include avoiding factors that increase baseline pulmonary vascular resistance (PVR), maintaining preload in an optimal range while avoiding fluid overload, and maximizing right ventricular oxygen delivery.[19]

The failing RV is exquisitely sensitive to afterload, so one of the key goals is to keep pulmonary artery pressure (PAP) as low as possible. Various factors during anesthesia and surgery can precipitate rapid hemodynamic decompensation,

so the choice of anesthetic technique is based on the specific requirements of the procedure and the likely impact on PVR and RV.[20]

In the present clinical case, it was decided to use peridural neuraxial block due to the lesser hemodynamic compromise and cardiovascular changes, the block was established gradually with a very slow titration of the local anesthetic (3 ml), with the achievement of a T5 block level. Current literature mentions that low-dose neuraxial anesthesia is recommended for most cardiac pregnant patients, unless there is absolute contraindication, however, it should be kept in mind that it may cause an acute reduction in systemic vascular resistance, resulting in a decrease in preload, cardiac output and systemic perfusion pressure that can negatively affect perfusion and RV function.[21] It can also cause bradycardia due to blockade of the cardioaccelerator fibers, so it should be done progressively until the minimum blockade necessary to complete the surgical procedure is achieved.[22]

Dávila Cabrera SF, et al. present a case report of a 23-year-old patient with obstetric history: G2, P1, A0, previous delivery without complications, who was admitted at 35. During her admission she presented clinical data compatible with unstable angina pectoris, so a transesophageal echocardiographic study (TTE) was performed, which reported moderate pulmonary hypertension with PSAP 66 mmHg, so medical treatment was started with Sildenafil 50 mg orally every 8 hours and she was scheduled for cesarean section. O. and is scheduled for cesarean section, in which peridural anesthesia is decided with a mixture of isobaric bupivacaine 0.5% 10 ml plus fentanyl 100 mcg, achieving 15 minutes later the desired anesthetic level with little motor blockade, at the birth of the baby was administered oxytocin 2.5 IU infusion achieving adequate uterine contraction and manual delivery of the placenta. Newborn with Apgar 9/9, patient discharged to ICU without vasopressor or inotropic support with spontaneous ventilation.[23]

In contrast to peridural block, Martínez Salazar GG, et al. present a clinical case of a 22-year-old female with 39.5 weeks of gestation + 23 mm ostium secundum ASD with untreated moderate pulmonary valvular stenosis. Echocardiogram was performed and reported dilatation of right chambers with severe pulmonary arterial hypertension, without the use of pulmonary vasodilator. The patient was admitted with dyspnea on small efforts, so it was decided to terminate the pregnancy with cesarean section. Mixed neuraxial blockade was applied with hyperbaric bupivacaine 6 mg, with morphine 150 mcg, sufentanil 5 mcg, and dexmedetomidine 5 mcg. Epidural block was retained for postoperative analgesia. Anesthetic level was achieved until T6. Mean arterial pressures were maintained at 85- 87 mm Hg, without the use of vasopressor, with spontaneous ventilation and supplemental oxygen with mask with reservoir at 5 lts per minute. Furosemide 10 mg and oxytocin 6 IU were administered. A single live product was obtained, without complications.[24]

The combined spinal-epidural technique offers the advantage of intrathecal analgesia due to its rapid onset and deep sensory and motor block, while the epidural block allows prolonging analgesia and postoperative pain control through an epidural catheter.[25] Mixed neuraxial blockade allows the use of adjuvants such as opioids to reduce the doses of local anesthetics and thus have a low incidence of arterial hypotension, and also avoids the use of drugs that depress myocardial function. Low doses of subarachnoid block or fractionated doses have been used safely in epidural anesthesia even in patients with Eisenmenger's syndrome.[24]

González Aguilar MA, et al presents the case of a 22-year-old female with a diagnosis of 34 weeks of pregnancy + VSD + severe pulmonary hypertension + CHF NYHA III, who was admitted with a productive cough 4 weeks ago, as well as dyspnea on medium effort. Physical examination revealed pallor of the integuments, IY grade I, auscultation with scattered fine rales, ejection systolic murmur intensity II/IV, mitral holosystolic murmur with reinforcement of the second pulmonary sound and extremities with edema +++, echocardiogram reporting perimembranous VSD with LVEF 65%, severe functional tricuspid insufficiency, severe pulmonary arterial hypertension, with pericardial effusion of approximately 500 ml. Balanced general anesthesia (BGA) was decided, sildenafil 50 mg was administered 1 h before starting the anesthetic procedure, anesthetic induction was perdormed with etomidate 15 mg, fentanyl 210 mcg, cisatracurium 5 mg, maintenance with Sevoflurane and fentanyl 100 mcg, carbetocin 100 mcg IV was used, with success. The patient was intubated and discharged to the ICU.[26]

General anesthesia is considered a potential period of instability, the goal is to achieve pain control to avoid sudden increases in sympathetic tone and RV afterload, so it is recommended that during induction and maintenance, anesthetic agents be selected based on their effects on systemic and pulmonary vascular resistance, slow administration and incremental dosing of anesthetic agents.[27]

Regarding ventilation, hypoxemia, hypercarbia and acidosis should be avoided, as these abnormalities worsen PVR and RV function. It is recommended to avoid positive pressure ventilation and high PEEP levels, because they may reduce venous return and right-sided cardiac output and a worsening of RV function, in extubation, it is advised to do it gradually with the use of pressure support (PS) ventilation mode.[28]

Balanced general anesthesia is not recommended due to the secondary hemodynamic effects of drugs and invasive mechanical ventilation that enhance hemodynamic decompensation; however, there are reports of cases where general anesthesia has been successful in the management of these patients.[29]

In both clinical cases previously described, Sildenafil was used; a selective inhibitor of phosphodiesterase 5, responsible for the intracellular hydrolysis of cGMP, it acts by enhancing

ON-mediated relaxation[30], it has been described as a good perioperative therapeutic option due to its greater availability and the fact that it significantly decreases PVR together with an increase in expulsive volume,[31] which was reflected in clinical improvement.

The uterotonic used in the present clinical case was a synthetic analog of oxytocin; however, the use of oxytocin by means of a continuous perfusion pump at the minimum dose that maintains effective uterine dynamics and does not cause volume overload, hypotension, tachycardia and increased cardiac output is recommended.[4] Prostaglandin E1 (intrarectal misoprostol 600 mcg) has comparable effects to oxytocin, without having the hemodynamic effects of oxytocin, however, fever, diarrhea and abdominal pain should be remembered.[32]

In the perioperative period, causes of acute hemodynamic decompensation should be avoided, as they can cause acute decompensated RV failure.

In our clinical case, the patient was admitted to the operating room with a state of hemodynamic instability due to the fact that she was in labor, a critical stage for the pregnant cardiac patient due to physiological stress and volume fluctuations, causing a significant decrease in the already limited cardiac output, exacerbating right heart failure.[33]

Perioperative increases in peripheral vascular resistance can be treated with inhaled nitric oxide, among other alternatives include pulmonary vasodilators (intravenous epoprostenol) or the administration of intravenous milrinone.[4]

The puerperium is the most critical time for the exacerbation of pulmonary hypertension, due to the increase in volume secondary to the extra blood supply due to uterine involution and the antidiuretic effect of oxytocin.[4] In the case of the patient, it is believed that the triggers that exacerbated the hemodynamic decompensation were the presence of transvaginal bleeding that the patient presented, as well as the greater demand for oxygen consumption when performing a rapid intubation sequence and the cardiovascular effects that this entails.

Most deaths in the immediate puerperium are due to refractory right heart failure, pulmonary hypertensive crisis, thromboembolism, volume depletion and preeclampsia.[4]

CONCLUSION

Pulmonary hypertension is defined as an increase in mean pulmonary artery pressure (PAP) > 25 mmHg at rest calculated by right heart catheterization, where the end result is right heart failure.

Timely diagnosis during pregnancy is of vital importance, as it is associated with high rates of maternal morbidity and mortality, so termination of pregnancy should be considered in all women regardless of functional class.

The goal of anesthetic management should be directed at keeping pulmonary artery pressure as low as possible. The use of epidural anesthesia implies minimal hemodynamic and respiratory changes compared to general anesthesia; however, both techniques are associated with a decrease in systemic vascular resistance, so anesthetic management is a challenge that should be individualized and should be performed by a multidisciplinary team.

REFERENCES

I. Galiè, N., Hoeper, M. M., Humbert, M., Torbicki, A., Vachiery, J.-L., Barberá, J. A., Beghetti, M., Corris, P., Gaine, S., Simon Gibbs, J., Gómez-Sánchez, M. Á., Jondeau, G., Klepetko, W., Opitz, C., Peacock, A., Rubin, L., Zellweger, M., & Simonneau, G. (2009). Guía de práctica clínica para el diagnóstico y tratamiento de la hipertensión pulmonar. Revista espanola de cardiologia, 62(12), 1464.e1-1464.e58. https://doi.org/10.1016/s0300-8932(09)73130-6

II. Simonneau, G., Gatzoulis, M. A., Adatia, I., Celermajer, D., Denton, C., Ghofrani, A., Gomez Sanchez, M. A., Krishna Kumar, R., Landzberg, M., Machado, R. F., Olschewski, H., Robbins, I. M., & Souza, R. (2013). Updated clinical classification of pulmonary hypertension. Journal of the American College of Cardiology, 62(25), D34–D41. https://doi.org/10.1016/j.jacc.2013.10.029

III. Lacassie Q., H. J., & r., y. M. V. (2013). HIPERTENSIÓN PULMONAR EN LA PACIENTE EMBARAZADA: MANEJO ANESTESIOLÓGICO PERIOPERATORIO. Revistachilenadeanestesia.cl. https://revistachilenadeanestesia.cl/PII/revchilanestv42n01.11.pdf

IV. Avellana, P., Segovia, J., López, F., Gómez-Bueno, M., García-Cosío Carmena, M. D., & Alonso-Pulpón, L. (2012). Hipertensión pulmonar y embarazo. Cardiocore, 47(4), 154–160. https://doi.org/10.1016/j.carcor.2012.03.002

V. Calderón-Colmenero, J., Sandoval Zárate, J., & Beltrán Gámez, M. (2015). Hipertensión pulmonar asociada a cardiopatías congénitas y síndrome de Eisenmenger. Archivos de cardiologia de Mexico, 85(1), 32–49. https://doi.org/10.1016/j.acmx.2014.11.008

VI. Humbert, M., Morrell, N. W., Archer, S. L., Stenmark, K. R., MacLean, M. R., Lang, I. M., Christman, B. W., Weir, E. K., Eickelberg, O., Voelkel, N. F., & Rabinovitch, M. (2004). Cellular and molecular pathobiology of pulmonary arterial hypertension. Journal of the American College of Cardiology, 43(12), S13–S24. https://doi.org/10.1016/j.jacc.2004.02.029

VII. Bassily-Marcus, A. M., Yuan, C., Oropello, J., Manasia, A., Kohli-Seth, R., & Benjamin, E. (2012). Pulmonary hypertension in pregnancy: Critical care management. Pulmonary Medicine, 2012, 1–9. https://doi.org/10.1155/2012/709407

VIII. Pieper, P. G., & Hoendermis, E. S. (2011). Pregnancy in women with pulmonary hypertension. Netherlands Heart Journal: Monthly Journal of the Netherlands Society of Cardiology and the Netherlands Heart Foundation, 19(12), 504–508. https://doi.org/10.1007/s12471-011-0219-9

IX. Smith, J. S., Mueller, J., & Daniels, C. J. (2012). Pulmonary arterial hypertension in the setting of pregnancy: A case series and standard treatment approach. Lung, 190(2), 155–160. https://doi.org/10.1007/s00408-011-9345-9

X. Sahni, S., Palkar, A. V., Rochelson, B. L., Kępa, W., & Talwar, A. (2015). Pregnancy and pulmonary arterial hypertension: A clinical conundrum. Pregnancy Hypertension, 5(2), 157–164. https://doi.org/10.1016/j.preghy.2015.01.004

XI. Olsson, K. M., & Channick, R. (2016). Pregnancy in pulmonary arterial hypertension. European Respiratory Review: An Official Journal of the European Respiratory Society, 25(142), 431–437. https://doi.org/10.1183/16000617.0079-2016

XII. Klinger, J. R., Elliott, C. G., Levine, D. J., Bossone, E., Duvall, L., Fagan, K., Frantsve-Hawley, J., Kawut, S. M., Ryan, J. J., Rosenzweig, E. B., Sederstrom, N., Steen, V. D., & Badesch, D. B. (2019). Therapy for pulmonary arterial hypertension in adults. Chest, 155(3), 565–586. https://doi.org/10.1016/j.chest.2018.11.030

XIII. Hemnes, A. R., Kiely, D. G., Cockrill, B. A., Safdar, Z., Wilson, V. J., Hazmi, M. A., Preston, I. R., MacLean, M. R., & Lahm, T. (2015). Statement on pregnancy in pulmonary hypertension from the pulmonary vascular research institute. Pulmonary Circulation, 5(3), 435–465. https://doi.org/10.1086/682230

XIV. Brassington, A.-M. E., Sung, S. S., Toydemir, R. M., Le, T., Roeder, A. D., Rutherford, A. E., Whitby, F. G., Jorde, L. B., & Bamshad, M. J. (2003). Expressivity of Holt-Oram syndrome is not predicted by TBX5 genotype. The American Journal of Human Genetics, 73(1), 74–85. https://doi.org/10.1086/376436

XV. Bonnet, D., Pelet, A., Legeai-Mallet, L., Sidi, D., Mathieu, M., Parent, P., Plauchu, H., Serville, F., Schinzel, A., Weissenbach, J., Kachaner, J., Munnich, A., & Lyonnet, S. (1994). A gene for Holt–Oram syndrome maps to the distal long arm of chromosome 12. Nature Genetics, 6(4), 405–408. https://doi.org/10.1038/ng0494-405

XVI. Fontecha Banegas, L., Moreno Alonso, I., & Huertas Patón, A. (2018). Síndrome de Holt-Oram y Trastorno del Espectro Autista. A propósito de un caso. Revista de psiquiatría infanto-juvenil, 35(4), 328–331. https://doi.org/10.31766/revpsij.v35n4a6

XVII. Murga-Eizagaechevarria, N., Garcia-Barcina, M., & Sarasola Diez, E. (2011). Síndrome de Holt Oram. Descripción de una familia afectada sin mutación del gen TBX5 ni manifestaciones en un probable transmisor. Revista espanola de cardiologia, 64(12), 1225–1226. https://doi.org/10.1016/j.recesp.2011.02.016

XVIII. Meucci, M. C., Malara, S., Butcher, S. C., Hirasawa, K., van der Kley, F., Lombardo, A., Aurigemma, C., Romagnoli, E., Trani, C., Massetti, M., Burzotta, F., Bax, J. J., Crea, F., Ajmone Marsan, N., & Graziani, F. (2023). Evolution and prognostic impact of right ventricular–pulmonary artery coupling after transcatheter aortic valve replacement. JACC. Cardiovascular Interventions, 16(13), 1612–1621. https://doi.org/10.1016/j.jcin.2023.05.003

XIX. Hector J. Lacassie Q. et al. (2013). Hipertensión pulmonar en la paciente embarazada: manejo anestesiológico perioperatorio. Rev Chil Anest, 42: 88-96. Hipertensión Pulmonar en la Paciente Embarazada: Manejo Anestesiológico Perioperatorio - Revista Chilena de Anestesia

XX. Arrigo, M., Huber, L. C., Winnik, S., Mikulicic, F., Guidetti, F., Frank, M., Flammer, A. J., & Ruschitzka, F. (2019). Insuficiencia ventricular derecha: fisiopatología, diagnóstico y tratamiento. Revisión de insuficiencia cardíaca, 5(3), 140–146. https://doi.org/10.15420/cfr.2019.15.2

XXI. Radaranida Gómez R, Claudio Nazar J. et al. (2013). Consideraciones generales de la embarazada con enfermedad cardiaca congénita y adquirida. Rev Chil Anest, 42: 77-87. revchilanestv42n01.10.pdf (revistachilenadeanestesia.cl)

XXII. Lacassie, H. J., De La Cuadra F., J. C., Kychenthal L., C., Irarrázaval M., M. J., & Altermatt C., F. (2021). Anestesia espinal parte V. Efectos fisiológicos. Revista chilena de anestesia, 50(4), 620–624. https://doi.org/10.25237/revchilanestv50-04-16

XXIII. Dávila Cabrera, S. F., Martínez Clavel, L. L., Hernández Román, M. A., Guerra Rosabal, L., & Montenegro Valhuerdi, A. (2021). Conducción anestésica perioperatoria en gestante a término con hipertensión pulmonar idiopática. Revista cubana de anestesiología y reanimación, 20(1). http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S1726-67182021000100009&lng=es&tlng=es

XXIV. Martínez-Salazar, G. G., & Martínez-Delgado, E. (2019). Embarazada con cardiopatía e hipertensión arterial pulmonar: Anestesia subaracnoideo: Descripción del caso. Anestesia en México, 31(1), 62–66. https://www.scielo.org.mx/scielo.php?script=sci_arttext&pid=S2448-87712019000100062&lng=es&tlng=es

XXV. Collis RE, Baxandall ML, et al. (1993). Combined spinal epidural analgesia with ability to walk throughout labour. The Lancet, 341: 767-768. https://doi.org/10.1016/0140-6736(93)90548-U

XXVI. González Aguilar M, García Valadez MB. (2021). Hipertensión pulmonar severa en embarazo: presentación de un caso. Revista Chilena de Anestesia; Sociedad de Anestesiología de Chile. 51 (6): https://revistachilenadeanestesia.cl/revchilanestv51 06101201/

XXVII. Pastor Torres, L. F., Antigao Ramírez, R., Honorato Pérez, J. M., Junquera Planas, C. M., Navarro Salas, E., Ortigosa Aso, F. J., Poveda Sierra, J. J., & Ribera Casado, J. M. (2001). Guías de práctica clínica de la Sociedad Española de Cardiología en la valoración del riesgo quirúrgico del paciente cardiópata sometido a cirugía no cardíaca. Revista espanola de cardiologia, 54(2), 186–193. https://www.revespcardiol.org/es-guias-practica-clinica-sociedad-espanola-articulo-13508

XXVIII. Benavides-Luna, H. M. (2017). Fisiopatología de la hipertensión arterial pulmonar. Revista colombiana de cardiologia, 24, 11–15. https://doi.org/10.1016/j.rccar.2017.07.001

XXIX. Beltrán-Gámez, M. E., Sandoval-Zárate, J., & Pulido, T. (2015). Inhibidores de fosfodiesterasa-5 para el tratamiento de la hipertensión arterial pulmonar. Archivos de cardiologia de Mexico, 85(3), 215–224. https://doi.org/10.1016/j.acmx.2015.03.001

XXX. Lewis, G. D., Shah, R., Shahzad, K., Camuso, J. M., Pappagianopoulos, P. P., Hung, J., Tawakol, A., Gerszten, R. E., Systrom, D. M., Bloch, K. D., & Semigran, M. J. (2007). Sildenafil improves exercise capacity and quality of life in patients with systolic heart failure and secondary pulmonary hypertension. Circulation, 116(14), 1555–1562. https://doi.org/10.1161/circulationaha.107.716373

XXXI. Lacassie Q., H. J., & r., y. M. V. (2013). Hipertensión pulmonar en la paciente embarazada: manejo anestesiológico perioperatorio. Revistachilenadeanestesia.cl. https://revistachilenadeanestesia.cl/PII/revchilanestv42n01.11.pdf

XXXII. Karam Toumeh d, et al. (2011) GPC. Diagnóstico y Manejo de la Cardiopatía en el embarazo. https://www.imss.gob.mx/sites/all/statics/guiasclinicas/538GRR.pdf

XXXIII. Galiè, N., Palazzini, M., Leci, E., & Manes, A. (2010). Estrategias terapéuticas actuales en la hipertensión arterial pulmonar. Revista espanola de cardiologia, 63(6), 708–724. https://doi.org/10.1016/s0300-8932(10)70163-9