Comments for ESPS Manuscript NO: 18694

We did review the paper by a professional English language editing company and we have attached the language certificate

1) General comments:

Transoesophageal echocardiography (TEE) is a possible and valuable tool in monitoring liver transplantation (LT), and its use by anaesthesiologists should be encouraged. This manuscript is interesting; however, I have some comments regarding the article.

2) Specific comments

a) Major comments：

# This review provided some useful information of TEE in clinical practice for physicians in monitoring LT. The authors described the application of TEE during LT in detail. However, although the procedure is generally safe, risks and benefits must be carefully weighted before TEE probe placement, as TEE is a semi-invasive method. There are a few inherent risks to placement of the probe, including pharyngeal and/or laryngeal trauma, dental injuries, esophageal trauma, bleeding, arrhythmias, respiratory distress and hemodynamic effects. Authors should not end with a word for this topic in Conclusion. More information needs to be added to the paper.

Answer

As rightly suggested by the reviewer we enriched the part of the text concerning the risks associated with the placement and use of the TEE probe, not limiting to address this topic only in the conclusion.

# So far, expert opinion on the use of TEE has not been consistent. Although some authors have advocated routine use during LT, others have emphasized the bleeding risk and have indicated that TEE can provide a useful adjunct to PAC in intraoperative hemodynamic monitoring during LT, especially in those patients at risk for cardiac complications due to pre-existing cardiovascular disease. Besides, TEE will not soon replace the use of PAC in the monitoring of perioperative hemodynamics during LT, because TEE does not provide the kind of hemodynamic information that is available from the PAC and is not as good at trending information (especially preload). I wonder how the authors would treat such situations

Answer

We totally agree with the reviewer. We have underlined in the text the limits of TEE and the advantages of PAC in trending information. We also expanded the comparison between the two techniques, explaining the benefits and limits of both.

As widely supported by literature, conventional pressure preload parameters did not adequately reflect left ventricular filling, indicating superiority of volumetric monitoring of cardiovascular volume status over conventional preload pressure monitoring[1-3]. The modified pulmonary artery catheter (CCOMBO-EDV) realizes this objective giving access to continuous volumetric preload assessment of the right heart. It allows continuous cardiac output and end-diastolic volume of the right heart measurements, which are better indicators of preload than cardiac filling pressure. However using right-heart catheterization for volumetric left ventricular preload assessment highlights some limitations. Right ventricular function differs considerably from left ventricular function. The major determinant of left ventricular function is myocardial wall tension, whereas for the right it is ventricular afterload[4]. Therefore, the relationship between right ventricular preload assessment and cardiac output readings may be weak. Another possible limitation of PAC use, comes from the patient

hemodynamic instability (arrhythmia/alteration of R waves) which make RVEDV/EF% to have a low predictive value in this case[5]. Some authors show that a patient heart rate major than 100 beats/min has a negative impact on the precision of PAC right ventricular ejection fraction measurement which is not observed with TEE evaluation[6], while other authors state the opposite, demonstrating that elevation of the heart rate results in larger errors on the TEE-derived CO estimate[7].

PAC monitoring reliability can be affected as well by thermal noise frequently witnessed before and after revascularization of the new graft, in case of peripheral or central venous massive fluid infusion, or unheated blood from the veno-venous by-pass[8, 9]. TEE, unlike PAC, is not affected by blood temperature changes and provides a calculated numerical value for left ventricular volume and cardiac output (e.g., by Simpson's rule) as well as a qualitative determination of right and left ventricular filling and ejection fraction.

Despite this advantage, also Transoesophageal echocardiography for monitoring left ventricular preload has some limitations which should be emphasized. Determination of the left ventricular end diastolic area index (LVEDAI) provides a measure of left ventricular filling that has been shown to correlate with changes in SV during volume therapy[10], only if the compliance and contractility of the left ventricle remain unchanged[11]. Quantitative assessment of left ventricular end-diastolic area by transoesophageal echocardiography may not necessarily reflect volume status due to myocardial wall motion abnormalities, and may be altered by dislocation of the probe from the midpapillary level[11].

TEE does not provide the kind of hemodynamic information that is available from the PAC especially in term of rapidity and continuity and is not as good at trending information (especially preload). Transoesophageal echocardiography application does not guarantee a continuous monitoring: no quantitative online evaluation of right ventricular function is available,

and only sporadic right ventricular ejection fraction values can be obtained [6]. For example, a sudden change in filling pressures or SvO2, as indirect indicator of cardiac output, is an extremely valuable information that allows the proper detection and identification of certain intraoperative events that TEE cannot offer[12]. Other authors argue instead that, unlike measurements obtained from a pulmonary artery catheter (3-6 minutes), which has delayed reactivity to rapid changes in cardiac output and intravascular volume, TEE allows immediate evaluation of contractility and preload in critical situations[12-14]

In comparison with pulmonary artery catheterization, TEE is a less invasive, but a technically more complex technique and for this reason qualified users are necessary in order to display standardized cross-sections and to interpret findings.[15] The technical complexity of TEE performance can be increased by the difficulty in obtaining short-axis visualization of the left ventricle, due to the common posterior retraction of the stomach during liver transplant, which requires preload to be determined mainly by the 4-chamber image[13]. Although TEE offers potential innovations in diagnostic imaging, there is a potential for serious misinterpretation, and inexperienced anaesthesiologists may confuse unfamiliar but normal anatomy as abnormal.

Beside this technical difficulty this method is either not practicable in a perioperative setting or cannot be routinely performed for logistic and economic reasons.

Until now, the available literature does not provide consistent answers on how to best monitor the hemodynamics during LT and whether a single monitoring device is superior to the others in terms of accuracy, validity and reproducibility of data. In other words, TEE does not replace the PAC at this moment and can be particularly useful when there is a specific condition (for example, cardiac disease and pulmonary hypertension). An excellent indication for PAC remains portopulmonary hypertension. Diagnosis and treatment of portopulmonary hypertension in patients undergoing LT

remains one of the strong indications for the insertion of a PAC, although a probate alternative may be the expert use of echocardiography[16]. Currently, echocardiography may provide slightly different information, so both monitoring devices could be used complementarily. De Wolf state that "we should aim for more direct monitoring of preload than filling pressures, and therefore the use of TEE and/or thermodilution-derived RVEDV should be encouraged".

# The language needs to be improved.

b) Minor comments

The minor comments are omitted.

References


1 Kumar A, Anel R, Bunnell E, Habet K, Zanotti S, Marshall S, Neumann A, Ali A, Cheang M, Kavinsky C, Parrillo JE. Pulmonary artery occlusion pressure and central venous pressure fail to predict ventricular filling volume, cardiac performance, or the response to volume infusion in normal subjects. *Critical care medicine* 2004; **32**(3): 691-699 [PMID: 15090949]

2 Cheatham ML, Block EF, Nelson LD, Safcsak K. Superior predictor of the hemodynamic response to fluid challenge in critically ill patients. *Chest* 1998; **114**(4): 1226-1227 [PMID: 9792607]

3 Diebel LN, Wilson RF, Tagett MG, Kline RA. End-diastolic volume. A better indicator of preload in the critically ill. *Archives of surgery* 1992; **127**(7): 817-821; discussion 821-812 [PMID: 1524482]

4 Hurford WE, Zapol WM. The right ventricle and critical illness: a review of anatomy, physiology, and clinical evaluation of its function. *Intensive care medicine* 1988; **14 Suppl 2**: 448-457 [PMID: 3042829]

5 Wagner JG, Leatherman JW. Right ventricular end-diastolic volume as a predictor of the hemodynamic response to a fluid challenge. *Chest* 1998; **113**(4): 1048-1054 [PMID: 9554646]

6 Zink W, Noll J, Rauch H, Bauer H, Desimone R, Martin E, Bottiger BW. Continuous assessment of right ventricular ejection fraction: new pulmonary artery catheter versus transoesophageal echocardiography. *Anaesthesia* 2004; **59**(11): 1126-1132 [PMID: 15479324 DOI: 10.1111/j.1365-2044.2004.03876.x]

7 Moller-Sorensen H, Graeser K, Hansen KL, Zemtsovski M, Sander EM, Nilsson JC. Measurements of cardiac output obtained with transesophageal

echocardiography and pulmonary artery thermodilution are not interchangeable. *Acta anaesthesiologica Scandinavica* 2014; **58**(1): 80-88 [PMID: 24192143 DOI: 10.1111/aas.12227]
8 Bottiger BW, Sinner B, Motsch J, Bach A, Bauer H, Martin E. Continuous versus intermittent thermodilution cardiac output measurement during orthotopic liver transplantation. *Anaesthesia* 1997; **52**(3): 207-214 [PMID: 9124659]
9 Bao FP, Wu J. Continuous versus bolus cardiac output monitoring during orthotopic liver transplantation. *Hepatobiliary Pancreat Dis Int* 2008; **7**(2): 138-144 [PMID: 18397847 DOI: 1076 [pii]]
10 Della Rocca G, Costa MG, Coccia C, Pompei L, Salandin V, Pierangelo DM, Pietropaoli P. Continuous right ventricular end-diastolic volume in comparison with left ventricular end-diastolic area. *European journal of anaesthesiology* 2009; **26**(4): 272-278 [PMID: 19276913 DOI: 10.1097/EJA.0b013e328319be8e]
11 Cheung AT, Savino JS, Weiss SJ, Aukburg SJ, Berlin JA. Echocardiographic and hemodynamic indexes of left ventricular preload in patients with normal and abnormal ventricular function. *Anesthesiology* 1994; **81**(2): 376-387 [PMID: 8053588]
12 De Wolf AM. Pulmonary artery catheter: rest in peace? Not just quite yet. *Liver transplantation : official publication of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society* 2008; **14**(7): 917-918 [PMID: 18581507 DOI: 10.1002/lt.21543]
13 Della Rocca G, Brondani A, Costa MG. Intraoperative hemodynamic monitoring during organ transplantation: what is new? *Current opinion in organ transplantation* 2009; **14**(3): 291-296 [PMID: 19448537 DOI: 10.1097/MOT.0b013e32832d927d]
14 Burtenshaw AJ, Isaac JL. The role of trans-oesophageal echocardiography for perioperative cardiovascular monitoring during orthotopic liver transplantation. *Liver transplantation : official publication of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society* 2006; **12**(11): 1577-1583 [PMID: 17058248 DOI: 10.1002/lt.20929]
15 Practice guidelines for perioperative transesophageal echocardiography. A report by the American Society of Anesthesiologists and the Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography. *Anesthesiology* 1996; **84**(4): 986-1006 [PMID: 8638856]
16 Della Rocca G, Costa MG, Coccia C, Pompei L, Pietropaoli P. Preload and haemodynamic assessment during liver transplantation: a comparison between the pulmonary artery catheter and transpulmonary indicator dilution techniques. *European journal of anaesthesiology* 2002; **19**(12): 868-875 [PMID: 12510905]