Reply to the Letter to the Editor

Reply to Ghosh et al.

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We would like to thank Professor Ghosh et al. [1] for their response to our systematic review [2]. It is well known that in our routine cardiac surgical practice transient low-cardiac output (LCO) state following mitral valve replacement (MVR) can occur. It has often been considered a complication of cardiopulmonary bypass and related to; intolerance to cardiopulmonary asystolic hypoxic arrest, reperfusion injury, inadequate myocardial protection, or a cardiopulmonary bypass associated systemic inflammatory response. Transient LCO state following mitral valve replacement can also occur for several other reasons: firstly due to an embolic phenomenon, for example, air emboli after inadequate de-airing; clot or particulate atheromatic emboli. Secondly, it can be due to metabolic causes such as hypoxia, hypercarbia, or electrolyte abnormalities. Thirdly, it can be related to conduction abnormalities and arrhythmias. Fourthly, it can be due to concomitant mechanical and technical failures, such as abnormal prosthetic valve function. Finally, transient low-cardiac output states can occur because of graft-flow related factors when simultaneous coronary artery bypass grafting is performed [3].

We agree with Professor Ghosh et al. that the association between Takotsubo syndrome and physiological or psychological stress [4] makes it an important differential alongside these recognized causes of low-cardiac output state following cardiac surgery. Particularly after mitral valve replacement, as the pathognomonic pattern of left-ventricular wall motion abnormality that occurs in Takotsubo syndrome resulting in left-ventricular apical ballooning may resemble sphericalization due to loss of mitral annuloventricular continuity [1]. Comparatively high estimates of the incidence of Takotsubo syndrome in patients presenting with acute coronary syndromes [4] suggest that Takotsubo syndrome is more common than previously thought, and may further implicate Takotsubo syndrome in the transient low-cardiac output syndrome that can occur after mitral valve replacement. The importance of Takotsubo syndrome after cardiac surgery needs to be better understood, and clearly further research is needed to quantify the incidence and risk factors for this syndrome. The important case study in which Takotsubo syndrome is described for the first time after cardiac surgery by Professor Ghosh’s group [5] was not included in our review of the literature [2] as it has only recently been published and was not available at the time of our literature search.

It is important to note however, that the incidence of low-cardiac output syndrome is markedly higher following mitral valve replacement when the mitral subvalvular apparatus are not preserved. Furthermore this effect, unlike Takotsubo syndrome, is often not reversible. This suggests that whilst Takotsubo syndrome may be an important differential when low-cardiac output occurs following mitral valve replacement, the predominant cause when the mitral subvalvular apparatus are not preserved is probably the disruption of annuloventricular continuity and ventricular geometry, resulting in permanent myocardial and valvular dysfunction [2].

References


Letter to the Editor

Are only serum creatinine levels good enough for detecting acute kidney injury?§

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I read with great interest the article titled ‘Does furosemide prevent renal dysfunction in high-risk cardiac surgical patients? Results of a double-blinded prospective randomised trial.’ [1]. First of all I would like to thank the authors for their efforts and then add a few things to the topic. We concur with the authors that perioperative urinary output more than 1 ml/kg/h is not an outstanding reflection of renal function after cardiopulmonary bypass. In that situation most of us think everything is all right. As the authors mentioned, lots of factors are responsible for acute kidney injury (AKI) for high-risk patients. Detection of AKI based on perioperative urinary output and several unreliable laboratory markers like serum creatinine underestimates the underlying renal status. Serum creatinine, although used routinely in clinical practice and in clinical trials, is a poor marker of renal dysfunction and an increase in which is not directly related to tubular injury in AKI. There is also a delay in the detectable increase in serum creatinine as a result of the time required for its accumulation.
and equilibration. Changes in creatinine can be nonspecific and may occur as a result of increased muscle mass and nutrition which are nonrenal factors. The alterations in serum creatinine are not particularly sensitive or specific for small changes in glomerular filtration rate [2].

Because of the vital importance of earlier targeting of therapies, many markers have been explored for early diagnosis of AKI. Although the initial studies on some molecules such as tubular enzymes, growth factors, adhesion molecules, and some cytokines were promising, the larger and the more detailed studies have shown an inadequate sensitivity or specificity to advocate its clinical use. Recently described molecules such as kidney injury molecule-1, neutrophil gelatinase-associated lipocalin, cysteine-rich protein 61 and IL-18 have demonstrated compelling results as markers of AKI at the preclinical level [2,3,5]. However, none of these molecules except lipocalin have been systematically explored in humans AKI. In a recent study, it was demonstrated that neutrophil gelatinase-associated lipocalin in the urine increases in pediatric patients after cardiac surgery before the increase in serum creatinine [2].

Nevertheless, the study did not comment on the severity or outcomes of AKI in these children. It has also been reported that serum cystatin C seems to increase 24—48 h before creatinine in patients with AKI but cystatin C is a marker of clearance and not a marker of renal tubular injury [4].

Over and above being a marker of renal tubular injury, urine IL-18 is an attractive test for further development as it is fast, reliable, accurate, and inexpensive. As compared with other markers, IL-18 has the advantage that it can be readily measured by commercially available ELISA kits. Availability of commercial kits can considerably hasten the development of the test for routine clinical use [5].

References


The authors of the original paper [1] were invited to comment on this Letter to the Editor but declined the offer.

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Results from the Italian CABG Outcome Project were published two years ago, generating controversial reactions among cardiac surgeons and a stimulating debate within the NHS.

Actually, the debate contributed to important advances in the systematic introduction of outcome evaluation and comparison within the Italian NHS. A national outcomes project has been developed since then; also a second round of the CABG study is currently ongoing, thanks to the key and enthusiastic cooperation of a significant number of Italian cardiac surgeons.

Apart from the expected dissent by professionals and hospitals whose performances resulted not so well, and their efforts to prevent us from publishing any kind of paper dealing with the Italian CABG Outcome Project, we know that the CABG study represents a substantial source of scientific evidence. Therefore, one year ago we published further papers dealing with the comparison of MLR and multilevel models in outcome studies and comparison between administrative and clinical databases [1,2]. On this specific occasion, we published a paper concerning the comparison between a local risk-adjustment model and the well-established EuroSCORE model [3].

We know Dr Menicanti never misses an opportunity to disagree with works dealing with the Italian CABG Outcome Project and, as in other previous occasions, his criticisms are directed towards the study per se rather than towards specific topics of the paper. Therefore, about 90% of the arisen questions are the same reported in other editorials concerning the Italian CABG study and which we have already largely replied to in previous published correspondences [4,5].

In this occasion we prefer to point out only a few issues.

The first is related to considerations about the study design. Actually, taking into account the objectives of the study, the appropriate study design was chosen before the study started. We confirm that a study designed as prospective does not become retrospective only because the data are analyzed some years after they have been collected.

The second deals with the citation from Dr Akins. We are sure the statistical analyses used in this paper are too elementary to be judged a ‘number torture’ to obtain the required results. The analyses only confirmed some expected results and led to already known considerations about the