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Coronary artery bypass grafting with minimal versus conventional extracorporeal circulation; an economic analysis☆

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ABSTRACT

Background: This study aims to develop a methodological framework for the comparative economic evaluation between Minimal Extracorporeal Circulation (MECC) versus conventional Extracorporeal Circulation (CECC) in patients undergoing coronary artery bypass grafting (CABG) in different healthcare systems. Moreover, we evaluate the cost-effectiveness ratio of alternative comparators in the healthcare setting of Greece, Germany, the Netherlands and Switzerland.
Methods: The effectiveness data utilized were derived from a recent meta-analysis which incorporated 24 randomized clinical trials. Total therapy cost per patient reflects all resources expensed in delivery of therapy and the management of any adverse events, including drugs, diagnostics tests, materials, devices, blood units, the utilization of operating theaters, intensive care units, and wards. Perioperative mortality was used as the primary health outcome to estimate life years gained in treatment arms. Bias-corrected uncertainty intervals were calculated using the percentile method of non-parametric Monte-Carlo simulation.
Results: The MECC circuit was more expensive than CECC, with a difference ranging from €180 to €600 depending on the country. However, in terms of total therapy cost per patient the comparison favored MECC in all countries. Specifically it was associated with a reduction of €635 in Greece, €297 in Germany, €1590 in the Netherlands and €375 in Switzerland. In terms of effectiveness, the total life-years gained were slightly higher in favor of MECC.
Conclusions: Surgery with MECC may be dominant (lower cost and higher effectiveness) compared to CECC in coronary revascularization procedures and therefore it represents an attractive new option relative to conventional extracorporeal circulation for CABG.

1. Introduction

The development of the heart–lung machine by John Gibbon in 1953 revolutionized cardiac surgery. Improvements in cardiopulmonary bypass (CPB) technology established the use of extracorporeal circulation (ECC) with aortic cross-clamping and cardioplegic arrest of the heart as the gold standard technique in performing open cardiac surgery. In coronary artery bypass grafting (CABG) procedures, CPB provides optimal conditions (a bloodless field and an arrested heart) for complete and accurate myocardial revascularization, while in intracardiac procedures, such as valve surgery or repair of structural defects, CPB is considered mandatory [1]. Advances and significant experience accumulated during the course of the past six decades, through a significant number of cardiac procedures performed under ECC worldwide, have contributed to improved health outcomes. This achievement was attained despite the increasing percentage of elderly and high-risk patients treated and has established the high level of quality and efficacy of modern heart surgery over the years [2].

The induction of systemic inflammatory response (SIRS) and the coagulation cascade constitute the major drawback of CPB, which is associated to end-organ injury postoperatively [3]. Various strategies have been developed in order to attenuate SIRS after cardiac surgery. Minimal ECC (MECC) was introduced in clinical practice in 1999 in order to improve the efficiency of the intervention. The main aim was to reduce the side effects caused by CPB, to result in a low inflammation response, as in the case of off-pump surgery, and to reduce the need for blood, while at the same time, to allow for a complete myocardial revascularization [4]. The rationale was to increase biocompatibility by utilization of a heparin-coated short circuit, to reduce foreign surfaces requiring low priming volume and to avoid air–blood interaction. Results obtained early from cohort observational studies and subsequently from small, single-center randomized studies, have demonstrated the value of MECC in reducing morbidity, by minimizing the deleterious effects of CPB [5]. A recent meta-analysis of 24 randomized studies comparing MECC to conventional ECC (CECC), with 2770 patients in total, detected a survival advantage with MECC in coronary procedures [6].

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Regarding the economics, it is important that, in the contemporary restrained economic situation, the introduction of any new therapeutic modality should, alongside proven efficacy, be associated with proven economic efficiency. To our knowledge, up-to-date there isn't any comprehensive economic evaluation focusing on the application of MECC in any healthcare system. Therefore, we performed the present health economic evaluation in order to assess the cost effectiveness of CABG with MECC relative to CECC in different European healthcare systems that have adopted MECC in their clinical practice, including Greece, Germany, the Netherlands and Switzerland. The use of MECC in these countries is more widespread and the number of cases undertaken in clinical practice account for the majority of cases undertaken worldwide.

2. Methods

2.1. Study objectives

The scope of this analysis is twofold. Firstly, we attempted the development of a general framework for assessing the benefits and costs of MECC versus CECC in various healthcare settings and perspectives. In addition, an economic evaluation was undertaken to compare MECC versus CECC in patients undergoing CABG in four healthcare settings: Greece, Germany, the Netherlands and Switzerland. The paper presents the results of this economic analysis.

2.2. Analysis perspective

The perspective of analysis is the point of view from which the costs and benefits are recorded and assessed. In the related health economic literature, the choice of perspective is justified and derived logically from the research question and the decision it designed to support and facilitate. In the literature, most often there are three different perspectives adopted. The "societal perspective" evaluates the benefits and costs of an intervention for society overall, whereas in the payer and the provider perspective the costs and benefits considered are only those incurred by them, respectively.

For the case of Greece and the rest of the countries, the economic evaluation was carried out from the perspective of the National Health System (NHS); hence, only direct healthcare provider costs were considered in the analysis. These are costs which are associated directly with the care of patients and reflect all the resources expensed in delivering the treatments under investigation and managing any adverse events within the healthcare system. Such resources concern the drugs, consumables, devices, diagnostic test consumed and the operating room, ward and human resource utilized to deliver each therapy under consideration. Moreover, they must also reflect the overhead cost which relates to electricity, cleaning, security, administration and all other supportive services allocated to the specific medical service delivered. Due to the question at hand and the perspective adopted, indirect costs such as lost productivity loss and any other non-medical costs borne by patients and/or their families were not considered in the analysis.

2.3. Effectiveness measurement

One of the most important elements in economic evaluation is the measurement of treatment effectiveness. It is important to use the right parameter which quantifies the impact of the intervention on patient health and to collect data from reliable sources. In most jurisdictions, the main effectiveness measure employed is life-years (LY) or quality adjusted life years (QALYs) gained as a result of delivering an intervention. In many cases only intermediate outcome parameters are available and, therefore, mathematical modeling is inevitably used to undertake survival extrapolations based on epidemiological data.

In terms of data quality and reliability, the hierarchy of studies proposes that randomized control trials represent the most robust source of effectiveness data, followed by meta-analyses and then observational studies. Nonetheless, each study design has its advantages and disadvantages. Trials for instance are very rigorous scientifically (high internal validity) but do not necessarily reflect properly real life situations and effects (low external validity). Observational data sets on the other hand reflect better real life, but are not as robust and rigorous as clinical trial. The major advantage of meta-analyses is that they combine data from different and often small studies and hence attain greater statistical power [7]. The effectiveness data used in the present economic evaluation came from a recent systematic review and meta-analysis, which incorporated 24 randomized clinical trials with 2770 patients in total [6]. In this study, MECC was defined as "a closed heparin-coated low-prime volume circuit, baring a centrifugal pump, with the absence of venous or cardiotomy reservoir precluding blood–air conduct". On the other hand, CECC was considered as "any system comprising an open venous reservoir with cardiotomy suction that collects shed blood and returns it into the circuit". The authors followed the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines [8] to evaluate the impact of MECC compared to CECC on mortality and major adverse cardiac and cerebrovascular events (MACCE) in patients undergoing heart surgery. Regarding the validity of eligible randomized studies included in the meta-analysis an experienced investigator determined the adequacy of randomization and concealment of allocation, blinding of patients, health care providers, data collectors and outcome assessors. Risk of bias was appraised according to the Cochrane risk of bias tool [6].

The study detected an improved short-term mortality and morbidity outcome in the MECC group [6]. The mortality rate quantified in the meta-analysis is the main health outcome measure considered here. In particular, perioperative mortality was used to estimate LYs gained with one treatment over the other. Because there are not available data regarding the long-term survival of patients in each treatment option, a conservative assumption was adopted. Namely, the horizon of the analysis was set at five years. Hence, it is assumed that the death rate in the surviving cohorts is the same and in this period the only difference in LYs is attributed entirely to the differences in perioperative mortality. This approach underestimates the survival benefit of the most effective therapy.

In general, the time frame of analysis should be long enough to capture all cost and benefit differences between treatments, relevant to the decision in hand. Thus, a longer time horizon could be considered more appropriate for the type of evaluation undertaken here. However, due to lack of appropriate long-term data on the effectiveness of comparators (especially for mortality), a shorter time horizon was chosen as a more reliable and conservative approach. Moreover, due to lack of appropriate data, quality of life was not considered in the present model. Nonetheless, it is reasonable to be assumed that quality of life may not differ significantly between the treatment arms, which in term imply that the better treatment in terms of LY would remain so in terms of QALYs, perhaps with a diminished benefit.

2.4. Cost measurement

In the original meta-analysis, several sub-analyses of treatment effects were conducted in the clinical evaluation of the two treatment strategies. However, from an economic point of view, only the effects which have meaningful economic implications for the NHS were considered. In addition, cost-effectiveness analysis is concerned in incremental effects; hence cost variables which implied an equal economic burden in both arms were excluded [9].

Total cost per patient in each arm accounts for the expenses associated with the delivery of treatment and the management of any major adverse event. Hence, in this context the total cost of therapy reflects the use of the intensive care unit (ICU), the use of inpatient ward for patient in-hospital stay, the cost of red blood cell (RBC) transfusion, the cost of intraaortic balloon pump used, the cost of mechanical ventilatory support and generally all other economically significant resources consumed. Table 1 presents all related data used in the deterministic and probabilistic analysis.

In order to estimate the cost of an RBC transfusion in Greece, a micro-costing bottom-up analysis was conducted. Specifically, the related cost reflects the resources expensed for blood collection and testing and the cost of transfusion itself. The cost of blood collection and testing accounts for the cost of transfusion bag, molecular HIV and hepatitis B/C testing, blood separation, group typing and storage. For the preparation of blood, 2 h work by technicians was considered based on expert advice. The cost of transfusion per patient reflects cross-matching, white blood cell removal filters and time required for the infusion. The average cost of transfusing one unit of blood was estimated at €906, which is in line with earlier estimates for the case of Greece [10]. The cost of RBC transfusion in the rest of the countries was estimated in a similar manner based on local expert advice and data. The numbers of blood units used per person are calculated based on data coming from the meta-analysis and are presented in Table 1.

In a recent study, it has been estimated that the hospital direct and overhead operating cost of a regular ward stay is €280 per day for an average unit in Greece [11]. Hence, total cost per case for each treatment arm was estimated by combining the above figure with the average length of stay. Apart from the cost attributed to the hospitalization in a regular ward, the use of ICU also represents an important cost driver in the case of CABG [12]. In theory, the ICU cost includes fixed costs and variable costs. Fixed costs exist no matter how many patients are treated and include depreciation for the initial and subsequent maintenance cost of the capital employed in the delivery of service. On the other hand, variable costs are dependent on the volume of services provided. Some costs, such as salaries of personnel, are fixed over a specific range of patient volume, but may change when the patient volume exceeds a specific range [13]. In the present context, the total cost for an ICU stay, accounts for the resources consumed by a regular patient, plus an additional cost for ancillary service, specifically for a mechanical ventilator.

A recent analysis showed that Greek hospitals suffer from major inefficiencies, which have significant impact on their operational ICU cost [14]. In this context a recent unpublished study conducted by the authors (data on file) estimated the mean local cost per day in ICU at €800 per day on average (staff costs excluded). Assuming that the cost is perfectly divisible and linearly correlated with length of stay, the cost of ICU stay per hour is estimated at €33.3 (€800/24 h), to match with available data from the meta-analysis employed. The ratio of the cost per day in ICU to the cost per day in a regular ward (2.85/1) is in line with those observed in other European countries (2.5/1 to 4/1 ratio) [14]. A 3.5% discount rate for all outcomes was used as a standard approach in this kind of studies. The cost for the rest of the countries was estimated in a similar manner, based on local data collected from experts in each country.

Regarding postoperative morbidity after CABG it is evident that postoperative complications, such as postoperative myocardial infarction, neurologic event or atrial fibrillation, normally occur with other secondary complications rather than in isolation. Incremental cost increase is attributed to the resources consumed for the management of the specific complication together with the cost attributed to increased length of ICU and hospital stay [15]. The cost of prolonged hospitalization accounts for the greater proportion of the total additional cost attributed to any complication. In the absence of universal