The paper from Ranucci et al. [1] presents a new system of recalibration of the logistic EuroSCORE to be used in high-risk cardiac patients. It has a great merit of highlighting the importance of regularly updating the predictive models and validating them at a local level. To keep up with the pace of new technologies and proposed therapies and in order to avoid misinterpretations of the results achieved in ongoing clinical trials, we should evaluate if the models available today are still valid. In addition, a localisation of a risk-assessment model makes it more valuable for actual decision makers who face real-life clinical situations in various environments. As both a medical doctor and a CMO of a medical device company, I recognise the value of customising a predictive model, especially when participating in the design of clinical studies. In addition to these points highlighted by Ranucci, an additional comment pertaining to the use of predictive models can be made. There might be a risk associated with inappropriately combining and analysing together discordant data when implementing different available predictive score models for different subsets of patients and diseases. This practice has sparked the current controversy regarding the appropriate models for patient selection and the associated patient outcome evaluation. Ranucci’s article, therefore, represents an opportunity for discussion about these and other aspects among all stakeholders.

According to the users’ perspective, there are several reasons to have and implement a predictive risk score [2]. Patients need objective criteria with which they can make their own judgement on a proposed therapy. Health professionals wish to compare their results to the standard of care taking into account the different case-mix, so as to improve the standards of quality within the health institutions [3]. Local administrations base their rank list on adjusted results before possibly taking a necessary corrective action. The reimbursement authorities, in order to validate the incremental benefit offered by different therapeutic options, should be presented with comparable data. Finally, medical device companies, when applying to the regulatory bodies for marketing approval of a new product, need to define the targeted patient population. Historically, predictive risk-score models have been conceived by different workgroups on the basis of the observed outcomes following a well-defined therapy applied in a particular subgroup of patients; [4] the presumption that they are exhaustively comprehensive for all possible patient subsets and available therapies has been invalidated [5,6]. For this reason, great caution should be exercised when trying to apply a predictive risk model for a purpose it was not originally intended for [7]. This becomes particularly relevant when comparing different therapeutic options applied by different health-care professionals to treat the same disease, as is the case currently with the treatment of aortic valve disease. Interventional cardiologists are focussing on transcatheter therapies; cardiac surgeons continue to trust the ‘gold standard’ surgical approach; and teams in a few major centres have integrated both functions into ‘valvular disease clinics’.

Various scores are comprised of different variables, giving each a different weight. Thus far no single model has proven to be ideal for the individual patient. Though a single model may be quite appropriate for the institution as a whole, a combination of different scoring models might represent, as proposed by different authors, the best possible solution. Combining pictures taken from different angles might offer in the end the best representation of a multifaceted reality and allow for the most accurate prediction of immediate and intermediate outcomes [8]. Patient demographics, pathology characteristics and specific therapeutic treatment chosen along with the operator’s own record should probably all be tracked if one wishes to give a customised estimate of the outcome [9,10]. In the surgical field, mortality has been used for decades as the most important surrogate of patient outcome. Mortality is uniquely relevant to the patient and objective to measure; the only point to be debated is the correct definition of in-hospital death. It has been demonstrated that STS-PROM is the most sensitive model for predicting increased overall mortality when patients are identified as high risk [11,12]. Misuse of currently available scores is of concern: unfavourable over-prediction may inadvertently make doctors deny surgery to patients who would otherwise do well with a standard surgical technique, even in the highest-risk cohort. On the other hand, an ideal model should also identify those patients for which any possible treatment would fail to improve their outcome. New treatments not only have provided new solutions to old.
problems but also have the potential to create new unattractive legacy: doctors are facing today previously unknown complications, whether related to the procedure, the delivery method or to the device itself that may be considered iatrogenic [13,14]. The final decision on treatment method rests with the patient. It is probably unethical to help a patient to make a final decision without providing objective data on the predicted mortality of the natural history of the disease versus that offered by the proposed treatment, and also the rate of untoward events. Indeed, the quality of life might be hampered by the evolution of the disease as much as by the collateral effects of the treatment. Today, more than ever before, outcomes other than mortality should be predicted by the ideal risk algorithm: both the patient and the society at large might value resumption of active life as important as survival. As procedural success rates have improved over the years, due to a better comprehension of patho-physiology and a perfection of technical skills, other metrics to better define success have been sought out: hospital length of stay, morbidity and recovery time, among others [15,16]. Some of these ‘soft measures’ focus on the patient’s general condition post-operatively, others are more ‘health-economic’ oriented and as such they are not necessarily congruent [17,18]. In light of new historical events, not to mention the current economic crisis, the concurrence of as many elements as possible should be our recipe for success [19]. Survival, avoidance of serious procedural and device-related complications, short hospitalisation periods, rapid return to work or active life, achievement of the acknowledged ‘gold standard’ therapeutic result and containment of overall treatment cost represent some of the ingredients that should always be present, regardless of the ‘chef’ and the pertaining area of specialisation.

Nevertheless, some confusion arises when comparing different therapeutic options where little clinical data exist for some of the options [20]. What you end up with are ‘apples and oranges’ comparison. The alternatives for transcatheter aortic valve implantation are presented as less invasive and, therefore, might look more appealing: avoidance of a surgical incision (provided this is the case) and no need for circulatory support (excluding stand-by, major rescues and conversions) should all improve the success rate. However, what is a successful outcome has not been yet defined. In fact, a blurred, self-defined mortality rate termed ‘not device/procedural-related’ is consistently affecting the survival curves of those who were successfully treated and survived the procedure, even though these patients are supposed to be ‘immune’ from complications related to the trauma and the cardiopulmonary bypass [21]. Noteworthy is the assertion that prognosis related to advanced age or severe concomitant diseases, which are common characteristics in the population of currently treated patients, would not be affected by the treatment. It appears therefore that the major impact of transcatheter therapies would be on the quality of life of the treated patients in comparison to the untreated population. Would this assumption still be valid when making a comparison with surgically treated patients? If so, what would be the result of a risk/benefit ratio addressing a younger patient population? Are patients and referring physicians prepared to accept a possible trade-off between invasiveness, long-term valve durability and clinical results? [22] Can the partial procedural success rate, the less than gold-standard results, the new iatrogenic complications, the high cost of new devices, related procedures, repeat procedures and logistics justify such a proposed paradigm shift? The STS score has proven to be more reliable when assessing high-risk patients [23]. Is this still true for lower risk patients?

Apparently, the final outcome will be influenced by a sum of different factors: the cardiac disease to be treated, the type of therapeutic procedure adopted and other concomitant diseases, among others. They will all affect the efficacy of the treatment, the survival and the quality of life of the patient. The relative weight of each factor might vary widely depending on different circumstances, making the choice of the most viable option, individualised and based on the needs of the single patient rather than being indiscriminately proposed to categories of patients. New therapies should only be part of the ‘armamentarium’ available to doctors, broadening their portfolio, rather than replacing well-established methods of treatment and narrowing the array of options available to them. Transcatheter therapies should be characterised as adjunctive tools to be used for a very specific and limited range of indications and not intended as an alternative therapy for all patients. Therefore, there is a clear need for a method to discriminate between those patients who would benefit the most from these new approaches and those who would unnecessarily be exposed to unknown risks. Last but not least, there is another dimension we should take into account: time. Classical devices/procedures used to treat valvular disease offer long-term proven results in terms of efficacy and safety [24,25]. The assumption is that after the immediate postoperative period the major risk is related to anticoagulation/thrombosis and structural valve deterioration issues; these will nevertheless be present with new devices as well. New device/procedure success might be hampered by variables whose effects have not yet been established, such as the persistence of the native valve which might affect the function and durability of the implanted device and jeopardise coronary flow. Therefore, not only we should try to predict the probability of peri-procedural and in-hospital mortality, the long-term survival and the number of patients who will return to an active lifestyle, but also add new criteria for evaluation such as freedom from reintervention (as would be the case for a valve-in-valve or surgical intervention), freedom from device structural deterioration and freedom from major cardiac adverse events, among others.

In recent years, we have learnt that a large proportion of people affected by valvular disease were not referred for any kind of intervention for different reasons. In this same period, some papers showed evidence of beneficial effects when treating patients at an early stage of disease [26–28]. These assumptions together created great expectations from both medical professionals and industry, apparently ‘out there’ there is a large unmet need that might create opportunities for both players. The implicit consideration was that old therapies would not be suitable for these new patients either because they were to be treated early in the course of their disease, or on the contrary, being at the
opposite end of the disease spectrum, they were in too severe a condition. In each of the two conditions, surgery is considered by some as too invasive irrespective of the excellent long-term results consistently proven over decades of activity on extremely large series. The spreading perception is that ‘less than perfect’ results, definitely considered inadequate only a short time ago, today become surprisingly neglectable, at least for patients deemed to be at the worst end of the gamut. Subsequently, there have been published analyses of referral patterns which proved to be, unexpectedly, too generous: patients who were either asymptomatic or not-severe enough were referred together with almost terminal patients [29, 30]. Many of these, considered initially too high risk for conventional surgery, were not amenable to alternative therapies and ultimately underwent classical therapies with excellent results. In fact, an undeniable merit of this new wave of patient scrutiny is clearly encouraging surgeons to push themselves even further and achieve optimal results in spite of critical preoperative conditions or peri-procedural emergencies. The final result is that the benchmark is higher today than it was only a few years ago. All of this did not require the setup of new expensive hybrid rooms, the sometimes-difficult interdisciplinary cooperation, time- and resource-consuming pre-procedural investigations or a major impact on the overall health-care budget.

Most likely this is just the start of a new era of valve surgery: the transapical approach might allow complex surgery to be performed in a predictable manner in the presence of uncontrollable aortas, and minimally invasive surgery will allow to lower the procedural impact and give better cosmosis, while assuring the best possible curative results and refusing to compromise on the final outcome [31, 32]. The renewal of the aortic valve bypass, through an apico-aortic valve conduit and the offspring of sutureless valve replacement allowing limited cardiopulmonary and clamp-off time, might allow the surgeon to approximate ‘zero impact’ [33, 34]. Surgeons at the end of this effervescent and competitive era might find themselves with sharpened skills and with an increased variety of equipment at their fingertips in such a way to offer the patient a tailored and predictable evidence-based therapy within an evidence-based health-care system.

References


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