Biomaterials 36 (2015) 6–25

Contents lists available at ScienceDirect

Biomaterials

journal homepage: www.elsevier.com/locate/biomaterials

Review

Polymeric heart valves for surgical implantation, catheter-based technologies and heart assist devices

Deon Bezuidenhout [a, b, *, 1], David F. Williams [b, c, 1], Peter Zilla [a, b, 1]

[a] Cardiovascular Research Unit, MRC IUCHRU, University of Cape Town, South Africa
[b] Strait Access Technologies Pty Ltd, Cape Town, South Africa
[c] Wake Forest Institute of Regenerative Medicine, NC, USA

ARTICLE INFO

Article history:
Received 1 July 2014
Accepted 12 September 2014
Available online 16 October 2014

Keywords:
Heart valve prostheses
Polymeric
Surgical
TAVI
LVAD

ABSTRACT

Efficient function and long-term durability without the need for anticoagulation, coupled with the ability to be accommodated in many different types of patient, are the principal requirements of replacement heart valves. Although the clinical use of valves appeared to have remained steady for several decades, the evolving demands for the elderly and frail patients typically encountered in the developed world, and the needs of much younger and poorer rheumatic heart disease patients in the developing world have now necessitated new paradigms for heart valve technologies and associated materials. This includes further consideration of durable elastomeric materials. The use of polymers to produce flexible leaflet valves that have the benefits of current commercial bioprosthetic and mechanical valves without any of their deficiencies has been held desirable since the mid 1950s. Much attention has been focused on thermoplastic polyurethanes in view of their generally good physico-chemical properties and versatility in processing, coupled with the improving biocompatibility and stability of recent formulations. Accelerated in vitro durability of between 600 and 1000 million cycles has been achieved using polycarbonate urethanes, and good resistance to degradation, calcification and thrombosis *in vivo* has been shown with some polysiloxane-based polyurethanes. Nevertheless, polymeric valves have remained relegated to use in temporary ventricular assist devices for bridging heart failure patients to transplantation. Some recent studies suggest that there is a greater degree of instability in thermoplastic materials than hitherto believed so that significant challenges remain in the search for the combination of durability and biocompatibility that would allow polymeric valves to become a clinical reality for surgical implantation. Perhaps more importantly, they could become candidates for use in situations where minimally invasive transcatheter procedures are used to replace diseased valves. Being amenable to relatively inexpensive mass production techniques, the attainment of this goal could benefit very large numbers of patients in developing and emerging countries who currently have no access to treatment for rheumatic heart disease that is so prevalent in these areas. This review discusses the evolution and current status of polymeric valves in wide-ranging circumstances.

1. Introduction

1.1. Background to heart valve disease and devices

While many factors determine the healthy functioning of the heart, most of them being electromechanical in nature, the ability of the valves of the heart to control, in an energetically favourable capacity, the flow of blood in and out of the heart and its chambers is of crucial significance. The failure of valves to carry out this function in certain disease states, especially as a consequence of the general ageing process, has been known for a long time, and the use of medical devices to effect greater control over blood flow represents one of the most important contributions that biomaterials

* Corresponding author. Cardiovascular Research Unit, Christiaan Barnard Division of Cardiothoracic Surgery, Faculty of Health Sciences, University of Cape Town, 203 Cape Heart Centre, Anzio Road, Observatory, 7925, Cape Town, South Africa. Tel.: +27 21 406 6476.
E-mail addresses: Deon.Bezuidenhout@uct.ac.za, deonbez@mweb.co.za (D. Bezuidenhout).

[1] All three authors declare a potential conflict of interest, being Directors of the company Strait Access Technologies, Cape Town, South Africa, that is developing technologies to treat rheumatic heart disease.

http://dx.doi.org/10.1016/j.biomaterials.2014.09.013
0142-9612/

and implantable devices have made to health care. Traditionally the patient population perceived to be at most risk have been the elderly individuals in the developed countries of North America, Europe and parts of Asia/Australasia, who suffer from the degenerative changes of either stenosis or incompetence. The age of patients in this group at first heart valve surgery has typically been in excess of 70 years, and a median freedom from valve-related complications of 15 years, has been considered to be a very satisfactory resolution to the problem. For several decades, the market for prosthetic heart valves, dominated by the needs of this patient cohort, has been considered to be mature and static.

However, the whole area of heart valve disease, and indeed heart failure itself, has been undergoing rapid change since the beginning of the twenty-first century, and there is now a perceived need for new types of devices. The circumstances relate to different ends of the age spectrum. At the elderly end of this spectrum, more and more individuals require valve replacement or repair, but, because of age or co-morbidities, are unsuitable for the open-heart surgery that is required for attention to the valves; this has caused an immense interest in minimally-invasive techniques and catheter delivered valves, whose structure and design has to be quite different to the normal surgically implanted prosthesis. Also, the ageing population has brought an increase in patients with serious heart failure conditions. For some time now, the technology has been available, albeit at very high cost, to allow artificial hearts or heart-assist devices to be used. There are many types of design, which has lead to some innovations of valve concepts, although not all of these devices actually utilize valves.

Secondly, and of far greater significance numerically, there is still an increasing number of young adults in the developing world who acquire rheumatic heart disease. Very many individuals in sub-Saharan Africa, and also in parts of Asia and South America suffer from this condition and they die when relatively young because of the damage that their heart valves sustain as a result of this disease. The availability of open-heart surgery, and of expensive prostheses, is extremely limited, such that new concepts and new devices for the treatment of these individuals has become an imperative. This situation is exacerbated by the fact that the changes to valve structure that occur in rheumatic heart disease, arising from inflammation, are different to the usual degeneration-induced changes in old age, so that procedures and devices may have to be different.

There is, therefore, a newly recognized need for larger numbers and different types of heart valve treatment. This may be seen from an estimate that the total number of patients requiring heart valves would triple, from 290,000 in 2003 to over 850,000 by 2050 based on population growth and ageing alone [1] and indeed, due to the previously under-estimated incidence of rheumatic heart disease in developing nations, this number is likely to be very much higher [2,3].

During the half-century of the clinical use of heart valve prostheses, several different types of material have been used in their construction, but for much of that time only a small number of generic constructs have been common, principally the metal-carbon combinations for mechanical valves and some treated animal tissues for the so-called bioprosthetic valves. Synthetic polymers rarely featured. They do, however, have some very attractive features and are likely to form the basis of new types of device. This review focuses on the development of such polymers and their prospects for the future. In doing so, these materials and devices have to be placed into the context of conventional and alternative materials.

1.2. Commercial heart valve prostheses

As with some surgical treatments of other parts of the cardiovascular system, it is possible to consider the use of transplanted tissue, in this case transplanted human valves. Such procedures, for example the Ross procedure that utilizes transplanted homograft pulmonary vales [4] represent an important place in the history of valve disease. Whether they are homograft or allograft, however, they constitute only a small percentage of procedures today due to limited availability and demanding surgical techniques.

There are two main types of commercially available prosthetic valves, the mechanical and bioprosthetic valves, and these account for the overwhelming majority of surgically implanted valves. While almost half of the implanted valves were mechanical in the late 1990s [5], more than 80% prostheses implanted in the industrialised world today are tissue valves [6,7]. Current tilting disc valves typically comprise annular rings containing mostly two pyrolytic carbon occluders; they have high durability but relatively un-physiological haemodynamics in terms of turbulence and shear stresses and consequently require lifelong anticoagulation due to the associated thrombogenicity [3,8]. Bioprosthetic valves consist of leaflets made from chemically treated animal valves or leaflets, or from animal derived pericardium; these valves may be stented or un-stented. Compared to mechanical valves they have better haemodynamics in view of their similarity to natural flexible leaflet valves, and do not require lifelong anticoagulation, but they do have limited durability due to calcification and degeneration processes [3,9]. As we note later, degeneration of valves is particularly aggressive and rapid in younger patients, including those with rheumatic heart disease. The bioprosthetic valves also have a smaller effective orifice area than current mechanical valves [10]. Although both types of valve do have their deficiencies, these are largely manageable, and cardiac surgeons do have a reasonable selection of devices for the vast majority of their eligible, aged patients; indeed there are widely used algorithms that advise on the choice of device on the basis of patient age and risk factors [11].

The one obvious drawback to surgically implanted valves is the self-evident need for open-heart surgery. This is expensive and not everyone with heart valve disease is well enough to be exposed to the procedure. For these reasons, transcatheter valves that can be delivered through minimally invasive techniques, through a vein or an artery or through the apex of the heart have recently been developed [12]. The aortic valve has been the usual target, with the procedures referred to as Transcatheter Aortic Valve Replacement (TAVR) or Implantation (TAVI). They were initially limited, by regulatory agencies, to the patients who were most at risk with open-heart surgery or young people in whom it was considered best to limit multiple open procedures [13,14], but these indications are now expanding [15]. Clinically employed transcatheter valves usually consist of collapsible/expandable metal stents containing soft leaflets similar to those used in surgically implantable bioprosthetic valves.

1.3. Availability and costs

Although we do not discuss the detailed economic aspects of heart valves here, these factors clearly play a role in the strategies for the technology development. Surgically implantable bioprosthetic and mechanical valves are expensive because of the R&D, clinical trial, regulatory, manufacturing and insurance costs. Bioprosthetic valves have the additional burden of the labour-intensive fabrication that requires hand sewing of tissues to frames. While these costs, when transferred to the prices of the finished product, may be bearable by many patients in many developed countries, that may not be so in poorer countries, even taking into account adjustment of costs to local economies.

There has been some success in the development and manufacture of valves within the developing countries themselves, exemplified by the Chitra valve made in India [16]. The occluders of