

Guest Editorial

Mechanical Circulatory Support Devices: Is It Time to Focus on the Complications, Instead of Building Another New Pump?



COMPLICATIONS—THE CATCH-22

... complications remain primarily patient related, not device related.

1994 Report—Combined Registry for the Clinical Use of Mechanical Ventricular Assist Pumps and the Total Artificial Heart

Millions of patients suffer from heart failure worldwide, with many dying each and every year. For over 60 years, scientists and clinicians from all over the world have been working on mechanical circulatory support (MCS) devices (total artificial hearts and ventricular assist devices using both pulsatile and nonpulsatile flow approaches). The results of this work impact only a small number of patients and are not really helping the millions of patients suffering from heart failure. Despite the significant advances, MCS remains largely the technology of last resort. Those actively involved in the field have witnessed the impressive potential of the technology; however, it remains a difficult sell as an earlier-stage intervention in the so-called less “sick” patients. It is that old “catch-22”; the rate of complications is simply too high to expose less sick patients to, and the rate of complications cannot be reduced in the moribund patients the technology is currently being utilized in, or can it be?

In 1994, the sixth and final official report of the Combined Registry for the Clinical Use of Mechani-

cal Ventricular Assist Pumps in Conjunction with Heart Transplantation was published (1). In that report, some of the most frequent complications were bleeding, infection, renal failure, respiratory failure, and neurological complications. Interestingly, the incidence of device malfunction (e.g., mechanical/electrical/technical problems) was relatively low, occurring in just 6.7% of all patients. Since that time, many new devices have been developed, with many entering the clinical arena. However, 13 years and thousands of MCS patients later, the latest data from the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) (2) has confirmed that the same complications continue to plague the use of MCS technology today. As aptly titled by Dr. Hunt in her recent editorial “New data, old problems” (3), the key issues facing the field remain largely the same. These same problems were identified many years ago; is it now time to implement a different strategy for helping the millions of suffering heart failure patients and those who die each year?

HISTORICAL COMPLICATION RATES

Figure 1 provides historical data on complications from the three major MCS registries:

- 1 Combined Registry for the Clinical Use of Mechanical Ventricular Assist Pumps and the Total Artificial Heart (1)
- 2 The Mechanical Circulatory Support Device Database (MCSDB), International Society for Heart and Lung Transplantation (4)
- 3 INTERMACS (2)

These data span an extensive time frame from 1985 to the present. Direct comparison of these data is extremely difficult, given the different definitions for complications, different patient populations, different device types, and different patient support durations, as well as many other related issues. However, the exercise certainly provides an interesting macro view

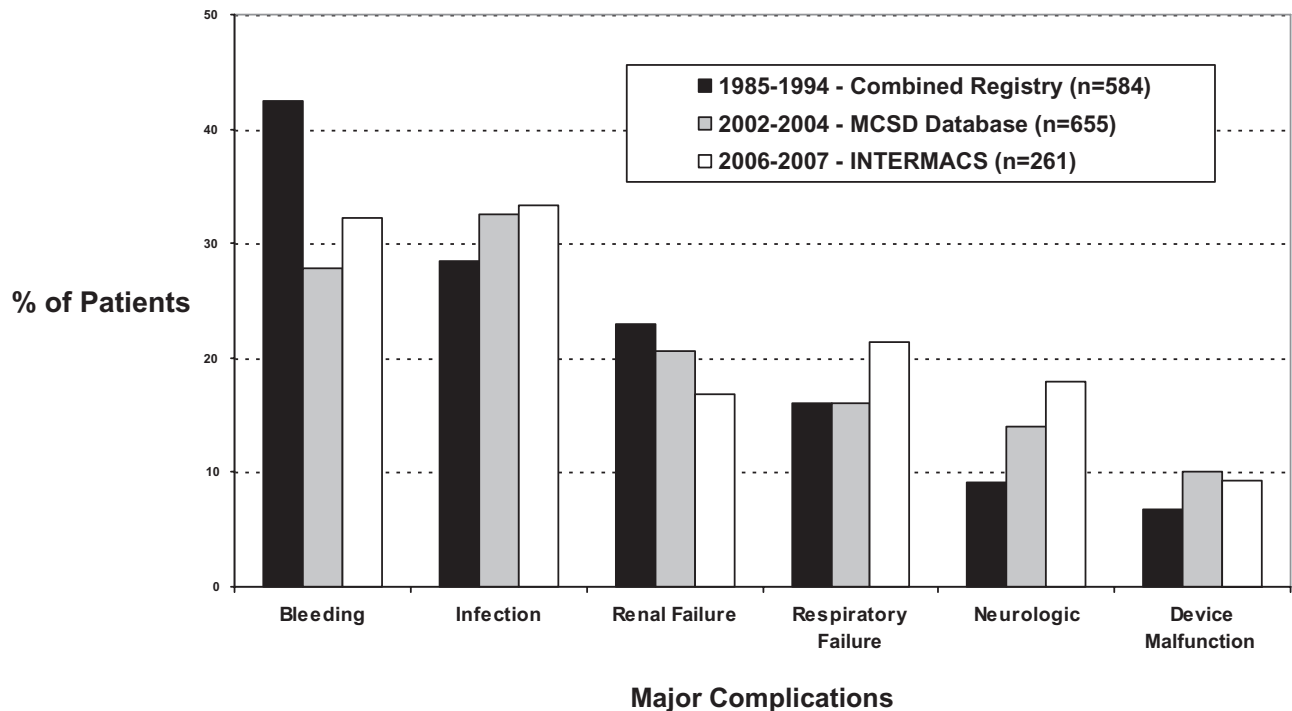


FIG. 1. Major complications of mechanical circulatory support.

of the overall progress in the field from the point of view of the serious complications typically facing MCS patients over this time period.

As seen in Fig. 1, with perhaps the exception of major bleeding, the incidence of most major complications has remained relatively consistent over time, at least from the available registry data and given the previously noted caveats. As device malfunction typically remains below 10%, and the other major complications such as infection have rates in the 20–30% range, perhaps greater scientific and clinical research focus is required on these complications, rather than simply bringing another new pump to market.

INFECTION—THE INSIDIOUS COMPLICATION

Infection remains one of the most insidious and frequent complications of MCS. Perhaps the most compelling data coming out of the Randomized Evaluation of Mechanical Assistance for Treatment of Congestive Heart Failure (REMATCH) study was related to infection. In REMATCH, sepsis was the most frequent cause of death (17 of 41 deaths) in the left ventricular assist device (LVAD) arm (5). Sepsis also played an important role in the reduced survival (60 vs. 39% at 1 year, 38 vs. 8% at 2 years) for LVAD patients without sepsis and those who experienced

sepsis, respectively (6). The cost modeling data from the REMATCH study further suggested that the incremental cost per patient with a device infection of the pump housing or sepsis was in the range of \$92 000–\$144 000 (7). Given the significant impact on morbidity, mortality, and cost, infection represents an important target for additional focused research and clinical strategies.

There is also new data suggesting serious concerns for late-onset driveline infections. In a retrospective study of 73 implantable LVAD recipients, late-onset driveline infections were noted for all patients with support durations over 1 year (8). Additionally, these infections resulted in significantly increased morbidity, and despite aggressive treatment often led to repeated surgical revision and serious pump pocket infections requiring either urgent transplantation or device explantation.

INFECTION CONTROL STRATEGIES

The good news is there are several promising infection control strategies outlined in the literature that are at least worthy of further investigation and/or potentially more widespread clinical utilization, as outlined further.

Pump pocket treatment

The use of a prophylactic antibiotic paste (vancomycin, collagen hemostat, and thrombin spray) in

pump pockets lowered pocket infection rates from 44% (19/43) to 12% (4/32) in a single-center retrospective study (9). This type of approach with a minimal cost (approximately \$135 per application) is certainly worthy of further follow-up.

Intraoperative device handling

The use of antibiotic-soaked sponges (e.g., vancomycin and gentamicin) to cover the device after assembly and prior to implantation, including on the driveline and cannulae, should now be standard practice (10). Additionally, irrigation of all surfaces should be performed with antibiotic-normal saline solution (e.g., vancomycin 2 g/L and gentamicin 160 mg/L) prior to close (11).

Lead treatments

Leads impregnated with antimicrobials may also reduce early infection and facilitate the in-growth of tissue to provide long-term stability and protection against late infection. In vivo studies of leads impregnated with chlorhexidine, triclosan, and silver sulfadiazine have demonstrated (i) a reduced incidence of microbial colonization from 100% (control leads) to 13% (impregnated leads); (ii) reduction of three orders of magnitude in bacterial adherence; and (iii) a 20-fold decrease in colony size at the lead exit site (12).

Implant site and antimicrobial barriers

The creation of an intraperitoneal pump pocket using expanded polytetrafluoroethylene (ePTFE) sheets containing antimicrobials (silver carbonate and chlorhexidine diacetate) has also demonstrated some potential for reducing pump pocket infections. A single-center study using historical controls found that pump pocket infection rate dropped from 31% (4/13) to 4% (1/25) in MCS patients (13). This study was confounded by several issues, including that the majority of the historical controls were abdominal wall implants (which may be more prone to infection) and that the investigators also implemented significant operative precautions including utilization of full hood-and-gown surgical suits and restricted access to the operating room. Nevertheless, the impressive overall results suggest that this approach is a worthy candidate for further clinical investigation.

Wound management

The use of calcium-sodium alginate dressings may also be helpful in treating percutaneous lead exit site deterioration in LVAD patients. In six LVAD patients with exudative wound deterioration, significant improvements were noted over standard wound care

through the use of calcium-sodium alginate dressings. Specific improvements included rapid and enhanced reduction in driveline separation, enhanced wound healing, and elimination of the need for subsequent surgical revision (14).

Transcutaneous energy transfer (TET)

While there has been some recent debate regarding the overall potential for TET technology to reduce infection and the cost associated with TET technology, there remains significant justification for further investigation. The first clinical data from totally implantable systems using TET technology including the AbioCor Total Heart (Abiomed, Danvers, MA, USA) and LionHeart LVAD (Arrow International, Reading, PA, USA) are just emerging. The AbioCor trial (n = 15) reports no device-related infections, no electrical interference or other problems related to electrical safety, and that the TET operation was effective for the duration of support (15). The LionHeart study (n = 23) reported infection in terms of comparisons with the REMATCH study, noting a 37% decrease in sepsis and a 26% decrease in septic death along with a 100% decrease in pump housing, inflow, and outflow tract infections (16). It was however noted that the incidence of local infections (including respiratory and urinary tract) was increased by 68%. This data is however extremely difficult to put in context, given the unique aspects of the LionHeart device with a significant number of implantable components and multiple implant sites and the relatively short implant duration compared with the REMATCH study. Regardless of these concerns, additional clinical study with TET systems is required to further elucidate the potential for reduction of infection along with the other associated benefits of TET technology (patient acceptability and quality-of-life issues).

Cellular coatings

Recent in vivo data concerning the adhesion of *Staphylococcus aureus*, one of the most common pathogens in MCS-related infections, also provides important knowledge regarding the pathogenesis of MCS-related infections (17). This work showed a 10-fold decrease in the adhesion of *S. aureus* to surfaces coated with endothelial cells when compared with surfaces coated with fibrinogen. This emerging knowledge could potentially be utilized to develop specific cellular coating approaches that limit biofilm formation on MCS devices.

Biofilm eradication via electrical impulses

Our own research group is actively investigating the use of weak electrical impulses to disrupt the structure of biofilm infections (18). This preliminary work sug-

gests that electrical impulses can potentially reduce biofilm resistance to antibiotics and inhibit bacterial growth. This approach may be especially useful to assist antibiotics and potentially host defenses to control and fight medical device biofilm infections.

CONCLUSIONS

Given the significant morbidity, mortality, and cost related to infection during MCS, greater efforts are required to address this insidious complication. There are many potential strategies, some of which have been highlighted herein. Most importantly, as noted by Holman et al., “institutional commitment to infection prevention can result in fewer infections” (10). Collectively, this same type of commitment is required by all those involved in the research, development, and clinical utilization of MCS devices. The overriding goal now needs to be focused on reduced complication rates, which will lead to a justifiable utilization in a less “sick” patient population. Building another new pump simply cannot accomplish this goal.

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Biographical Sketch

Dr. Mussivand’s areas of interest and contributions include artificial hearts (mechanical circulatory support devices) as treatment for heart failure, remote power transfer for implantable medical devices, remote patient monitoring (telemedicine), biofluid dynamics to reduce/eliminate thrombosis in blood conducting devices, patient care simulation center, detection devices and methods for detection, in situ sterilization, medical devices (failure analysis and regulatory process), and medical sensors. Combining his scientific, management, and business expertise, Dr. Mussivand has been the Chairman of several boards, member of various Boards of Directors, and the CEO of several successful corporations. Dr. Mussivand has published over 250 papers, books, and technical articles and supervised and taught over 300 students, residents, and postdoctoral Fellows. Presently, he is Professor of Surgery and Engineering at the University of Ottawa and Carleton University;

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