PERFORMANCE OF RE-USED PACEMAKERS AND IMPLANTABLE CARDIOVETER DEFIBRILLATORS COMPARED WITH NEW DEVICES AT GROOTE SCHUUR HOSPITAL, CAPE TOWN, SOUTH AFRICA

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ABREVIATIONS

AIDS: Acquired immune deficiency syndrome

AV: Atrioventricular

COPD: Chronic obstructive pulmonary diseases

CVA: Cerebro-vascular accident

FDA: Food and drug administration

HIV: Human immunodeficiency virus

ICD: Implantable cardioverter defibrillator

IQR: Interquartile range

LMIC: Low and middle income countries

NYHA: New York Heart Association

PMHYH: Project my heart your heart

$: Dollars

UK: United Kingdom

US: United States

USA: United States of America

DECLARATION OF ORIGINALITY

I, **ZIMASA VUYO JAMA** declare that this is my original work. Neither the whole work nor any part of it has been, is being, or is to be submitted for another degree to any other university. None of this work has been published in any format prior to registration for the abovementioned degree.

Signature.. Signed by candidate

Date: 24/04/2015

Abstract

Objectives: Little is known about the performance of re-used pacemakers and implantable cardioverter defibrillators (ICDs) in Africa. We sought to compare the risk of infection and the rate of malfunction of re-used pacemakers and ICDs with new devices at Groote Schuur Hospital in Cape Town, South Africa.

Methods: This was a retrospective case comparison study of performance of re-used pacemakers and ICDs in comparison with new devices at Groote Schuur hospital over a 10 year period. The outcomes were incidence of device infection, device malfunction, early battery depletion, and device removal due to infection, malfunction, or early battery depletion.

Results: Data for 126 devices implanted in 126 patients between 2003 and 2013 were analysed, of which 102 (81%) were pacemakers (51 re-used and 51 new) and 24 (19%) were ICDs (12 re-used and 12 new). There was no device infection, malfunction, early battery depletion or device removal in either the re-used or new pacemaker groups over the median follow up of 15.1 months (interquartile range (IQR), 1.3-36.24 months) for re-used pacemakers and 55.8 months (IQR, 20.3-77.8 months) for new pacemakers. In the ICD group, no device infection occurred over a median follow up of 35.9 months (IQR, 17.0-70.9 months) for re-used ICDs and 45.7 months (IQR, 37.6-53.7 months) for new ICDs. One device delivered inappropriate shocks which resolved without intervention and no harm to the patient, this re-used ICD subsequently needed generator replacement 14months later. In both, the pacemaker and ICD groups, there were no procedure non related infections documented for the respective follow up periods.

Conclusion: No significant differences were found in performance between re-used and new pacemakers and ICDs with respect to infection rates, device malfunction, battery life and

device removal for complications. Pacemaker and ICD reuse is feasible and safe and is a viable option for patients with bradyarrhythmias and tachyarrthythmias.

PART 1: LITERATURE REVIEW

Background

Pacemaker and implantable cardioverter defibrillator (ICD) implantation is an effective tool to treat bradyarrhythmias and life threatening tachyarrhythmias. The challenge with pacing and ICD use is the high cost of the devices. The high cost of pacemakers and ICDs has resulted in limited access of these life-saving interventions to deserving patients in developing countries.[1]

Epidemiology

Cardiovascular disease is the primary cause of mortality worldwide, accounting for 30% of all global deaths,[1] of which more than 80% of these deaths occur in people living in underprivileged/low and middle-income countries (LMIC).[1] LMICs are defined by the World Bank as countries that are generating a gross national income per capita that is lower than US$9200.[1-3] Mortality attributable to cardiovascular disease is double the mortality rate of HIV/AIDS, malaria, and tuberculosis combined worldwide.[4] There have been a declined in morbidity and mortality attributable to cardiovascular disease in recent decades as a result of improvements in technology and a greater emphasis on primary and secondary preventative strategies in the developed world.[1, 5] It is unfortunate that in LMICs this dramatic improvement in disease burden has not been witnessed.[1, 6]

In LMICs, secondary treatments are often limited because of the lack of skilled healthcare providers and more importantly, financial burden where by the patients are unable to afford costly medical procedures.[4]

This disparity in medical health care is evident in the field of cardiac electrophysiology, specifically pacemaker and ICD implantation.[1]

This specialty is either severely underdeveloped or entirely non-existent in many LMICs.[7] This results in suffering and death of patients with symptomatic bradycardia who cannot afford these devices or have no access to appropriate services (personal correspondence, University of Philippines-Philippines General Hospital, 15 November 2008).[1]

In South Africa, public health care services are tax funded and provide service at all levels of the health system.[8-11] People using public health care services have to pay a fee related to their income except for pregnant women and children under the age of six years.[11] Because of the diversion of funds from tertiary health care facilities to the primary care level, budgetary constraints to provision of tertiary services like cardiac surgery, cardiology and other expensive services have been witnessed.[11]

Review

Scott Millar et al[8] conducted a survey of cardiac pacing in South Africa in 1998 and identified a total of 1,643 new pacemakers implanted by 112 doctors working at 31 institutions (9 public centres and 22 private centres).[8] They reported an increase of 25.8% annual implant rate from 31 per million population in 1995 to 39 per million population in 1998 with 31.7% primary pacemaker implants in public sector in 1998 compared to 37 % in 1995.[8]

There was a huge difference between public and private sector practice with regards to indications of pacemaker implantation and type of pacemaker implanted due mainly to affordability, with the public sector being mostly where the financial burden was being observed.[8] In the public sector, atrioventricular (AV) block was the main indication for pacing in 75.3% of cases as opposed to 45.3% in the private sector,[8] whereas sinus node dysfunction accounted for 34.9% in the private sector as opposed to 16.2% in the public sector.[8]

Single-chamber pacemakers were the most utilised devices in the public sector and accounted for 49.5% of public sector implants as opposed to only 9.6% in private sector.[8] On the other hand reverse was true concerning dual-chamber implants with 12.1% implants in the public sector versus 42.3% in the private sector being dual chamber.[8] This difference as alluded above was because of the difference in budgets between the two sectors. Dual-chamber devices are more expensive compared to single chamber pacemakers, and sinus node dysfunction is predominantly left untreated provided is asymptomatic in the public sector.

Because of the difference in socio-economic status between racial groups in South Africa, there was an observed difference in implantation rates between them.[8] There were 232 per million implants in the white population as opposed to 8.8 per million implants in the black population.[8] Regional differences also exist due to uneven distribution and lack of trained and skilled implanters in some parts of the country.[8] The Western Cape had 89.3 per million population implants as compared to 10.8 per million population in the four provinces within the country without pacemaker implanters.[8]

Despite the growth of implants from 1995 to 1998, the pacemaker implantation rate is still lower than the developed world. The South African implant rate remains low at 39 per million population compared to the median implant rate of 283 per million in Europe.[8] This discrepancy is attributed to socio-economic factors that play a prominent role in the uneven and unequal distribution of this highly effective treatment for potentially lethal bradyarrhythmias.[8-9]

Mayosi et al[10] conducted a survey in the sub-Saharan region north of South Africa to determine the distribution of implanters and changing trends in pacing practice during 1995. Cameroon, Ghana, Ivory Coast, Kenya, Mauritius, Namibia, Nigeria, Senegal, Seychelles and Zimbabwe were the only countries in sub-Saharan Africa identified to have permanent pacemaker implanting centres.[10] This survey showed an increase in the number of countries with cardiac pacing centres in the sub-Saharan region north of South Africa (from 3 countries in 1981 to 10 countries in 1995).[10]

Mayosi et al[11] in 2002 tried to ascertain the utilization of ICDs in Africa through an electronic mail survey of cardiologists working in West, Central and East Africa and demonstrated that South Africa was the only country in Africa in which ICD implantation was being practised. This survey showed yet another increase in primary pacemaker implantation rate from 39 per million population in 1998 to 41 per million population in 2001, whilst the ICD implantation rate were 0.8 per million population.[11] The majority of the ICDs implanted in 2001 were privately funded with only 3 of the 35 implants that were implanted in a public hospital (Groote Schuur hospital) after a direct appeal to the authorities to fund the devices.[11]

Severe financial constraints prevented implantation of these devices by public hospitals, even those with the necessary expertise.[11] Marked regional and racial differences in implantation rates were identified, reflecting large socio-economic disparities between different regions and groups.[8-9] The rural black South Africans were the one severely affected due to poor access to health care in general and sophisticated tertiary health care in particular.[11]

Mond et al[7] in the 2005 World Survey of Cardiac Pacing and Cardioverter-Defibrillators demonstrated that the rates of new pacemaker implants in the United States of America (USA), Canada and Western Europe were over 380 per million population with USA having the highest rates at 752 per million populations compared to the underprivileged countries with 54 per million population in South Africa, 22 per million population in Thailand, 14 per million population in Peru and 4 per million population in Bangladesh.[7] ICD implantation showed similar results with USA having 401 per million population new implants as opposed to South Africa with 2 per million population, 3 per million population in Thailand, <1 per million population in Peru and Bangladesh.[7]

Mond et al[12] in the 2009 Worldwide Cardiac Pacing and ICD survey (Table 1 and 2) demonstrated that all countries participated in that survey showed an increase in the numbers of implant over the 4 year period from previous survey in 2005. This was the largest pacing and ICD survey ever performed encompasses more than 80% of all the pacemakers and ICDs implanted worldwide, with about sixty one countries contributed to the survey: 25 European countries, 20 Asian Pacific countries, 7 Middle East and African countries and 9 states in the USA.[12]

This survey included about 1,002,664 pacemakers of which 737,840 were new implants and 264,824 were replacements.[12] The USA had the largest number of pacemaker implants of 225,567 while Germany had the highest number of new pacemaker implants (927 per million population) Table 1.[12]

That survey also involved 328,027 ICDs of which 222,407 were new ICD implants while 105,620 were generator replacements.[12] All countries that participated showed a significant increase in the use of ICDs with the USA having the highest number of implants of 133,262 which corresponded to 434 implants per million population (Table 2).[12]

As Scott Millar et al[8] has shown in the South African survey in 1998 that atrioventricular block and sinus node dysfunction were the major indications for pacemaker implantation in the public sector and private sector respectively. This survey demonstrated the same result. Single chamber pacemakers were predominantly being utilised in the developing countries.[12] Dual chamber implants showed an increase in comparison to 2005 survey in all countries which were surveyed.[12] South Africa and Sudan were the only African countries participated in the survey.[12]

The high cost of these devices is attributed to the observed disparity between countries as shown in the table 1 and 2. As the cost of these devices differs with type or function of the devices, the pacemaker pulse generator at its most basic form costs around $2.500-3.000 and leads cost around $800-1.000, whereas ICD generator costs range from $20.000-40.000 and leads cost over $10.000.[13] Clearly underprivileged countries with meagre health care budgets will not afford these devices for everyone in need who cannot buy their own device, hence sterilization and reuse of these devices deserves consideration.

Pacemaker implantation is a lifesaving intervention for patients suffering from bradyarrhythmias.[14] Death from untreated atrioventricular block is not only due to heart failure secondary to low cardiac output, but also to sudden cardiac death caused by prolonged asystole or bradycardia triggered ventricular tachyarrhythmia.[15]

Patients with acquired complete atrioventricular block have a very poor prognosis with 1-year survival rates only between 50-70% compared to sex and age-matched controls, after atrioventricular block related syncope.[16-22] Although formal randomised controlled trials of pacing atrioventricular block have not be performed, it is clear from observational studies that pacing prevents recurrence of syncope and improves survival.[15]

Due to high cost of these devices, patients in underprivileged countries where there is no full medical coverage in place to buy the devices suffer and die because they cannot afford these devices. It was thought that donation of new devices by various charities to these countries would be the solution to this problem but the demand of these devices exceeds what these charities can offer.[14]

In order to overcome the unmet demand and address the disparity between countries, cadaveric donation of these devices is thought to be an option for these patients in these countries.[14, 23-32] Reuse of cardiac pacemakers has been practiced since the early 1970's.[33] It remains an option for those countries who cannot afford new devices.[14, 23-32] These devices are carefully selected and sterilised for reuse. [14, 23-32] At the moment there are no standardized protocols for sterilization of these devices, most centres follow chemical sterilization with biozyme and/ or orthozyme, followed by gas sterilization with ethylene oxide to meet the standards of that particular hospital's sterilization unit.

Pacemaker reuse is being practiced in many countries like India, Romania, Philippines, Canada, Australia, Italy, Sweden, Holland, Norway, Brazil, Hungary, Finland and Israel.[23] To the best of my knowledge, there is no publication on this practice in Africa.

This practice has raised concerns of device infection and malfunction.[28-29, 35-40] There are several factors associated with a greater risk of cardiovascular implantable electronic device infection (1) immunosuppression; (2) oral anticoagulation use; (3) patient coexisting illnesses; (4) peri-procedural factors, including the failure to administer peri-operative antibiotics; (5) device revision/replacement; (6) amount of indwelling hardware; (7) operator experience.[41] In recent years studies have been conducted to address these concerns about this practice. [14, 23-32]

Staphylococcus aureus is the most common culprit isolated in the vast majority of cases, and to a lesser extent coagulase-negative staphylococci (staphylococcus epidermis).[42-51] Antibiotic use at the time of implantation has significantly reduced the incidence of implant associated infections. Da Costa et al, in a meta-analysis of seven randomised-controlled trials, studying the effectiveness of systemic prophylactic antibiotics in reducing pacemaker-related infections, demonstrated that antibiotic use at the time of implantation significantly reduced the incidence of implant associated infections (combined odds ratio 0.256, p=0.046).[42] Klug et al demonstrated a significant reduction in infections related to pacemakers (N=5866) and cardioverter-defibrillators (n=453) implantations, in a study of 6319 implants with systemic prophylactic antibiotics at implantation (odds ratio 0.4).[43]

Oliveira et al in a study of 649 conservative patients randomised to either 1g intravenous cefazolin or placebo showed that prophylactic antibiotic use significantly reduced the incidence of infection (relative risk 0.19, p=0.016).[50] There are no guidelines on systemic prophylactic antibiotic use during pacemaker implantation, and the decision on whether to use antibiotics is usually at the discretion of the operator.[51] Due to the lack of studies comparing specific antibiotic regimens and their efficacy against device infection.[51]

Different centres use different antibiotic regimens.[51] It is difficult to evaluate a superior regimen, antibiotic that covers staphylococcus aureus as it is the main culprit is recommended.[51] Narrow spectrum antibiotics with staphylococci species coverage are preferred because of the risk of antibiotic associated diarrhoeas associated with broad spectrum antibiotics.

Flucloxacillin alone appears to be the most common regimen, intra-pocket gentamycin is also used in some centres.[51] Both regimes rarely cause clostridium difficile associated diarrhoea.[52-54] Most expert advocate cefazolin for prophylaxis.[41] But single dose cefazolin is known to cause clostridium difficile associated diarrhoea.[55-56] There are no randomised-controlled trials studying the effectiveness of prophylactic intra-pocket gentamycin in pacemaker implantation, this practice still needs further studies.[51]

There is a wide variation in the duration of antibiotic use post implantation, Dwivedi et al demonstrated that short course is just as effective as a longer course in preventing device infections,[44] but this still needs to be further studied. Preoperative antiseptic preparation of the skin of the surgical site and intra-procedural compulsive attention to sterile technique is mandatory in catheterization laboratories.[41] Haematoma formation prevention is mandatory post operatively.[41]

Professional associations have shown support of this practice. The National Association for Sport and Physical Education in 1985 supported the practice and considered it as a reasonably safe practice.[57] The American College of Cardiology/American Heart Association/National Association for Sport and Physical Education later acknowledged in 2002 that pacemaker reuse "may eventually add significantly to the cost-effectiveness of cardiac pacing".[58]

Currently, Food and Drug administration (FDA) regulations prohibit device reutilization as it is regulated as a class III device that is not to undergo re-sterilization with subsequent distribution.[59] Shipping of these devices unprocessed (as a hazardous material with no intention of human use) to the recipient country or institution, leaving the responsibility of sterilization and testing to the recipient institution was one of the proposed methods to address regulatory concerns but this placed a heavy burden on the underprivileged country.[60] Another approach is to file for FDA approval for potential exportation of re-sterilized devices only to those in need in undeserved nations.[61-62]

At present, Project My Heart-Your-Heart (PMHYH) is working with the FDA in order to provide a legal framework in the form of an investigational device exemption for those interested in providing this valuable resource to those in underserved nations.[60] This practice seems to be an answer to those in need but cannot afford new device. Device infection is the most feared complication of this practice,[47, 63-64] but there appears to be no significant difference in infection or mortality rates between reused and new device implantation.[24, 64-66]

Linde et al[24] reported a two year Swedish experience of pacemaker reuse. They conducted a retrospective case-control study of 100 consecutive patients who received re-used pacemakers either as a primary implant or replacement.[24] The patients who received re-used pacemakers (i.e., re-used pacemaker group) were matched by date of implantation and pacing mode (e.g., AAI, VVI, DDD) to 100 patients that received new pacemakers (i.e., new pacemaker group) to investigate the safety of re-use of pacemakers.[24] These patients were followed up over 32±11 months (means± standard deviation) for complications (e.g. pacemaker infections, pacemaker malfunction and early pacemaker replacement due to early battery depletion). The re-used pacemaker group was significantly older than the new pacemaker group (79±9 versus 68±21 years; $P<0.0001$).[24]

Results revealed a 3% complication rate in re-used pacemaker group versus 7% in the new pacemaker group (Table 3).[24] Eight of the complications that occurred were from primary implants (1=re-used pacemaker and 7=new pacemakers) and the rest (two) from replacements (2=re-used pacemakers).[24] The new pacemaker group had slightly higher infections as compared to the re-used pacemaker group.[24] One of the nine infections occurred before the era of routine intravenous antibiotics prophylaxis before pacemaker implantation.[24] There were no pacemaker generator replacements due to early battery depletion during the 32±11 months follow up.[24]

Panja et al[25] reported an Indian experience in a study of 642 patients with re-used pacemakers and the same number of new pacemakers looking to investigate infection rates between the two groups. 522 pacemakers in the re-used pacemaker group were pacemakers that were taken out of the same patient for whatever reason either infected or erosion or pre erosion, 120 were taken from cadaveric donation.[25] These pacemakers were sterilized and 522 were implanted back to the patients they were taken out from on the opposite side from the original site and 120 were implanted to patients who never had a pacemaker before.[25]

Their results showed that pacemakers reuse in the same patient had higher infection rate of 11.8% compared to cadaveric donated ones (5.1%) or new pacemaker implants (5.3%) over a follow up period of 7.5±5.6 years.[25] This higher infection rate in the same patient implant was attributed to lymphatic or haematogenous spread from the previous infected pocket rather than implantation of the previous explanted device as a key risk factor.[25]

Rosengarten et al[26] reported a Canadian experience in a prospective trial of new versus refurbished cardiac pacemakers. They implanted 70 pacemakers of which 52 (75%) were new and 18 (25%) were refurbished. The refurbished pacemakers were implanted in older patients with a mean± standard deviation age of 77±8 versus 69±13 years (P< 0.02).[26]
The rate of pacemaker related complications were the same in both groups over a follow-up period of 36 months, with 12 (23%) complications in the new pacemaker group and 4 (22%) complications in the refurbished pacemaker group.[26]

There were no major pacemaker related complications, early pacemaker battery depletions or pacemaker related deaths and this practice of refurbished pacemakers was shown to be cost effective and saved $33,000.[26] After three years the cumulative probability of survival in the new group was higher (P = 0.08).[26] New and refurbished pacemakers were similar with respect to pacemaker related survival and complications.[26] Refurbished pacemakers effect a major reduction in pacemaker costs while maintaining health care standards.[26]
Kantharia et al[29] found no significant complications in an Indian study cohort of 53 patients who received cadaveric donated sterilized pacemakers over a mean follow up of 661 days.

Catanchin et al[47] conducted an Australian retrospective pacemaker and ICD infection analysis: of 10 years of experience between 1994-2004 and reported an infection rate of 1.6%. Second or subsequent procedures carried a greater infection risk and mortality rate of 2.6% over mean follow up of 29.3 months.[47]

Pavri et al[67] reported an Indian experience of reuse of sterilized ICDs in a single centre retrospective cohort study. They found no device-related infectious complications and 60.4%

of the re-implanted devices delivered life-saving shocks or antitachycardia pacing to the recipient over a mean follow-up of 825 days.

Baman et al[23] conducted a meta-analysis of studies published looking at outcomes of pacemaker reuse from 1970 to 2010 aiming to assess safety of pacemaker reuse. They included about 18 studies with total number of 2270 patients.[23] The primary outcome of this meta-analysis was device infection or erosion with device malfunction as secondary end point.[23]They reported an infection rate of 1.97% (1.15%- 3%) associated with pacemaker reuse and device malfunction rate of 0.68% (0.27%- 1.28%), but there was no statistical significant difference in infection rates between new and re-used devices.[23] Device malfunction was much higher for pacemaker reuse compared to new pacemakers with P=0.02 that is statistical significant.[23]

Limitations of this meta-analysis should be taken into account when interpreting these results, which are as follows: (1) of the 18 studies analysed, only 5 of them had direct comparison of reuse and new devices;[23] (2) three of the studies included were published in an abstract form;[23] (3) none of the included studies were randomised controlled trials;[23] (4) the infection was not sub-classified into type and time of occurrence.[14] Regarding higher malfunction, device screw issues either during explantation or implantation of these device contributed to the difference in malfunction between the two groups, careful selection and testing of these devices prior to sterilization and implantation seem to have decrease the difference.[14]

Nava et al[14] conducted an ambispective noninferiority study to address the issue of efficacy and safety of pacemaker reuse in a study of 603 (307 in study group and 296 controls) consecutive patients from year 2000 to 2010 to examine short and long term performance of

pacemaker reuse. From 2000 to 2005 the study was retrospective and from year 2006 to 2010 it was prospective.[14] They assessed three major outcomes as a combined end point (device infection, device malfunction or unexpected battery depletion) over a follow up period of 4.10 years for the study group and 4.16 from controls.[14]

They found no statistically significant difference in infection rate and unexpected battery depletion between the two groups, and one device was found to be malfunctioning in the study group and no malfunction reported in controls.[14] The malfunctioning of that device was due to a faulty screw. This problem was eliminated after a policy of careful fault inspection and testing prior to sterilization was introduced.[14]

Conclusion

From the above literature review, pacemaker and ICD reuse compared with new devices seem to have no significant difference in respect to device infection but there may be higher rate of device malfunction associated with device reuse. Due to the absence of randomised controlled trials in this subject of pacemaker and ICD reuse, the safety and effectiveness of pacemaker and ICD reuse remains uncertain. To the best of my knowledge, no studies of the performance and safety of re-used pacemakers and ICDs have been conducted in Africa. This has prompted us to review and report our experience in Groote Schuur Hospital, Cape Town, South Africa with regard to the performance of re-used pacemaker and ICDs in comparison with new devices over the past decade (2003 to 2013).

Table 1: Cardiac Pacing 2009 compared to 2005[12]

Country	Population (million)	Number of centres (2005 survey)	New implants (2005 survey)	New implants Per Million centre (2005 survey)
Europe				
German	82	986	~76.046	927
France	62	550 (575)	~48.487 (44.915)	782 (738)
UK	62	211 (191)	32.135 (26.930)	518 (447)
Asia Pacific				
Australia	22	111 (123)	12.523 (11.850)	565 (590)
China	1.300	783 (417)	40.728 (16.595)	31 (13)
India	1.200	738 (417)	20.000 (12.000)	17 (7)
Africa/Middle East				
South Africa	49	(47)	2.939 (2.515)	60 (54)
Sudan	39	4	180	5
Iran	72	54 (41)	3.373 (2.529)	47 (37)
America				
USA	307	3.400	232.567 (223.425)	767 (752)
Argentina	40	600	11.478 (10.876)	287 (294)
Brazil	184	317 (252)	24.966 (19.071)	136 (103)

(2005 survey) = comparison with 2005 survey; UK= United Kingdom; USA= United States of America

Table 2: Implantable Cardioverter Defibrillators 2009 compared to 2005[12]

Country	New implants (2005 survey)	New implants Per Million Population (2005 survey)
Europe		
German	~23.752	290
France	~6.720	108
UK	~5.990 (2.835)	97 (47)
Asia Pacific		
Australia	3.555 (2.864)	160 (142)
China	1.316 (186)	1 (<1)
India	1.100 (415)	1 (<1)
Africa/Middle East		
South Africa	308 (105)	6 (2)
Sudan	2	< 1
Iran	1,260 (314)	18 (5)
America		
USA	133.262 (119.121)	434 (401)
Argentina	2.250 (672)	56 (18)
Brazil	2.825 (1.413)	15 (8)

(2005 survey) = comparison with 2005 survey; UK= United Kingdom; USA= United States of America

Table 3[24]

Number of complications during the study period

Pacemaker	Infection	Malfunction	Total
New pacemaker group	7	0	7
Re-used pacemaker group	2	1	3

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PART 2: THE MANUSCRIPT

PERFORMANCE OF RE-USED PACEMAKERS AND IMPLANTABLE CARDIOVETER DEFIBRILLATORS COMPARED WITH NEW DEVICES AT GROOTE SCHUUR HOSPITAL IN CAPE TOWN, SOUTH AFRICA

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Abstract

Objectives: Little is known about the performance of re-used pacemakers and implantable cardioverter defibrillators (ICDs) in Africa. We sought to compare the risk of infection and the rate of malfunction of re-used pacemakers and ICDs with new devices at Groote Schuur Hospital in Cape Town, South Africa.

Methods: This was a retrospective case comparison study of performance of re-used pacemakers and ICDs in comparison with new devices at Groote Schuur hospital over a 10 year period. The outcomes were incidence of device infection, device malfunction, early battery depletion, and device removal due to infection, malfunction, or early battery depletion.

Results: Data for 126 devices implanted in 126 patients between 2003 and 2013 were analysed, of which 102 (81%) were pacemakers (51 re-used and 51 new) and 24 (19%) were ICDs (12 re-used and 12 new). There was no device infection, malfunction, early battery depletion or device removal in either the re-used or new pacemaker groups over the median follow up of 15.1 months [interquartile range (IQR), 1.3-36.24 months] for re-used pacemakers and 55.8 months (IQR, 20.3-77.8 months) for new pacemakers. In the ICD group, no device infection occurred over a median follow up of 35.9 months (IQR, 17.0-70.9 months) for re-used ICDs and 45.7 months (IQR, 37.6-53.7 months) for new ICDs. One device delivered inappropriate shocks which resolved without intervention and no harm to the patient, this re-used ICD subsequently needed generator replacement 14months later. In both, the pacemaker and ICD groups, there were no procedure non related infections documented for the respective follow up periods.

Conclusion: No significant differences were found in performance between re-used and new pacemakers and ICDs with respect to infection rates, device malfunction, battery life and

device removal for complications. Pacemaker and ICD reuse is feasible and safe and is a viable option for patients with bradyarrhythmias and tachyarrthythmias.

Introduction

Pacemaker implantation is an effective tool to treat bradyarrhythmias, and implantable cardioverter defibrillators (ICD) reduce mortality in patients at high risk of sudden death.[1] The challenge with pacemakers and ICDs is the high cost of these devices. The pacemaker generator in its most basic form costs US$ 2.500-3.000 and leads cost US$800-1.000.[2] An ICD generator costs US$ 20.000-40.000 and leads cost over US$10.000.[2] The high cost of pacemakers and ICDs has resulted in limited access of deserving patients in poor countries of these life-saving interventions.[3-5]

Mond et al.[6] demonstrated an increase in pacemaker and ICD implantation rates in all countries that participated in the World Survey of Cardiac Pacing in 2009. Despite this increase in implantation rates, there was a huge difference in the number of implants between the developed and underprivileged countries, with more implants in the developed world.[6] This disparity was explained mainly by the high cost of these devices.[6]

Reuse of cardiac pacemakers has been practiced since the early 1970's.[7] The major concern with this practice is the risk of device infection and malfunction.[8-11] Device infection is the most feared complication of cardiac device reuse and is thought to be associated with case fatality rate between 2.6 to 18%.[12-14] However, some studies from America, Europe and Asia that examined the performance of re-used pacemakers and ICDs have shown no significant difference in infection or mortality rates between patients who received re-used and new devices.[14-22]

The aim of this study was to investigate the performance of re-used pacemakers and ICDs at Groote Schuur Hospital, Cape Town, South Africa.

Methods

This was a retrospective case comparison study of performance of re-used versus new pacemakers and ICDs at Groote Schuur Hospital, Cape Town, South Africa. We included consecutive devices that were implanted between 01 January 2003 and 01 January 2013. As shown in Fig. 1, there were 1721 devices implanted during that time, of which 1587 (92.2%) were pacemakers and 134 (7.8%) were ICDs. Of the 1587 pacemakers, 1257 (79.2%) were new implants and 330 (20.8%) were generator replacements. Of the 134 ICDs, 114 (85.1%) were new implants and 20 (14.9%) were generator replacements.

There were 54 (3.4%) re-used pacemakers and 12 (9%) re-used ICDs implanted during this period, with a total number of 66 (3.8%) re-used devices implanted as shown in Fig. 1. Patients with re-used devices (i.e., cases) were then matched by age, gender and date of implantation on 1:1 basis to patients with new devices (i.e., controls). In the pacemaker group, cases and controls were matched to the same month of implantation, and for the ICD group, to the same year of implantation.

Criteria for reuse

Devices for reuse were obtained from cadaveric donors. They were inspected for external damage and tested for remaining battery life. Devices with less than two years of battery life remaining and/or with external evidence of damage were not re-used. Only devices with two or more years of battery life remaining with no evidence of external damage were eligible for reuse.

The eligible devices were sterilised by immersion in biozyme for 24 hours, followed by peroxide for further 24 hours and then orthozyme for another 24 hours. After the three days of chemical treatment, the devices were dried out using pressurised air and subsequently

subjected to gas sterilization. In the gas sterilization unit, they were put in a machine with ethylene oxide for 4.5 hours and irradiated for two cycles of 30 minutes three days apart. After device sterilisation, all devices were checked by a cardiac technologist in the department for any visual defects, device longevity and were tested to determine if they were functioning appropriately for reuse. Device manufacturer's personnel were not involved in this process. A cardiac technologist or cardiology registrar in training was present at every implant procedure. Standard measurements were obtained during the implant after lead positioning (capture thresholds, battery life, sensitivities, and lead impedances) and again prior to discharge. Defibrillation testing was performed in all ICDs post implantation and all were functioning well with appropriate thresholds.

Re-used pacemakers were implanted mainly in elderly patients with multiple co-morbidities such as advanced cancer (on treatment or in remission), cerebro-vascular accident (CVA), advanced chronic obstructive pulmonary disease (COPD), dementia and/or a poor baseline level of functioning (mostly bed bound) who were expected to have a significantly reduced life expectancy. Re-used ICDs were implanted in patients who met the secondary prevention criteria for sudden death and co-morbidity was not a factor in determining who received a re-used ICD. The inherent difference between patients who received re-used pacemakers compared to those who had new pacemakers, led us not to compare the outcome of patients in the two groups. The units of analysis were devices themselves. Every patient provided a written informed consent for implantation of the device.

Implantation Procedure and Follow-up

Devices were implanted by a cardiac electrophysiologist, cardiologist or a cardiology senior registrar. Prior to implantation, patients received 1gram of intravenous infusion of cefazolin as prophylaxis. Patients were discharged from hospital the following day provided there were no complications and were followed up in the Pacemaker Clinic at 3 months and yearly thereafter. Patients with ICDs were followed up more frequently at 3-4 monthly intervals

Outcomes

The outcomes of interest were procedure-related infection, device malfunction, early battery depletion, and device explantation for infection, malfunction and/or battery depletion.

The definitions of the outcomes are as follows:

Procedure-related infection:

Infections were classified into four types:[23]

(1) Right sided endocarditis with lead involvement; (2) Sepsis with evidence of involvement of the lead and implantation pocket; (3) Involvement of pacemaker implantation pocket; and (4) Involvement of lead or generator.

Infections were considered early if the onset of illness was within the first month of implantation, and late if the onset of illness was after the first month to a year after implantation.[23] Infections that occurred after a year of implantation were considered not to be related to the procedure.[23] It is thought that procedure related infection manifests within the first year of implantation, and infection thereafter is considered not to be related to the procedure.[24]

Device malfunction

Device malfunction was defined as failure of the device to accomplish a desired role, e.g., in case of an ICD, not able to sense ventricular tachycardia/fibrillation and deliver appropriate treatment. In case of a pacemaker, device malfunction was defined as inability to sense or pace when required.

Early battery depletion

Early battery depletion was defined as battery depletion within 6 years of implantation for new devices. For re-used devices, early battery depletion was defined as battery depletion within 1-2 years of implantation for those with 2-4 years battery life remaining, and within 2 years of implantation for those with 4 years or more battery life remaining at the time of implantation, provided this depletion was not explained by high pacing outputs or abnormal electrode impedance.

Device explantation for infection, malfunction and/or battery depletion

Removal of the pacemaker or ICD for infection, malfunction or early battery depletion

Data extraction

The cardiac Clinic Electrophysiology Database was used to identify the cases with re-used devices and controls with new devices. Data were extracted from clinical notes in the Cardiac Clinic and additional information from pacemaker cards in the Cardiac Catheterization Laboratory and clinical records. Patient status was taken from clinical notes, the hospital electronic record (Clinicom) and the records of the Department of Home Affairs.

Statistical analysis

Categorical data were summarized as proportions and continuous data as means and standard deviations or medians and inter-quartile range. Categorical data were compared using the $\chi 2$ test, and continuous data using t-test or Mann-Whitney test. All tests were two-sided and a p-value of <0.05 was considered significant. IBM SPSS (version 19, IBM Corp., NY, USA) was used to perform the analysis.

Results

Three patients with re-used pacemakers were excluded from the analysis because of missing records. Data for 126 devices inserted in 126 patients between 2003 and 2013 were analysed, of which 102 (81%) were pacemakers (51 re-used and 51 new) and 24 (19%) were ICDs (12 re-used and 12 new). For the pacemaker group the median follow up for patients with re-used devices (i.e., cases) was 15.1 months [interquartile range (IQR), 1.3-36.24 months] and for those with new devices (i.e., controls) was 55.8 months (IQR, 20.3-77.8 months).

In the ICD group the median follow up for patients with re-used devices (i.e., cases) was 35.9 months (IQR, 17.0-70.9 months) and those with new devices (i.e., controls) was 45.7 months (IQR, 37.6-53.7 months).

Baseline characteristics of patients who received pacemakers are shown in Table 1 and pacemaker parameters are shown in Table 2. As expected re-used pacemaker cases had more significant co-morbidities compared to pacemaker controls. They were more likely to have advanced cancer, cerebro-vascular accident (CVA), advanced COPD and dementia with a poor baseline level of functioning mainly bed bound (due to CVA, dementia, atherosclerotic and diabetic vasculopathies with lower limb amputations and arthritis).

There were no differences between the two groups with respect to pacemaker parameters as shown in Table 2.

Baseline characteristics of patients who received ICDs are shown in Table 3 and there were no significant differences between the two groups. ICD parameters are shown in Table 4 and there were no significant differences between the two groups.

The pacemaker group was analysed separately from the ICD group. In the pacemaker group there were no device infections, pacemaker malfunction, early battery depletion or explantation of pacemaker due to infection, malfunction and early battery depletion identified after a median follow up of 15.1 months (IQR, 1.3-36.24 months) for cases and 55.8 months (IQR, 20.3-77.8 months) for controls. There were no procedure non related infections documented for this follow up period.

For pacemaker cases, 10 (19.6%) patients were followed up for 5years and more, 18 (35.3%) for 1-5 years and 23 (45.1%) for less than a year. For pacemaker controls 23 (45.1%) patients were followed up for 5 years and more, 21 (41.2%) for 1-5 years and 7 (13.7%) for less than a year.

In the ICD group, there was one device in the re-used device group that delivered inappropriate shocks (i.e., inappropriate delivery of shocks for supraventricular tachycardia), during the early stages of implantation but this resolved without any intervention. This device subsequently needed generator replacement after 14 months from implantation. There were no device infections identified after a median follow up of 35.9 months (IQR, 17.0-70.9 months) for cases and 45.7 months (IQR, 37.6-53.7 months) for controls. There were no procedure non related infections documented for this follow up period.

For ICD cases, 5 (41.7%) patients were followed up for 5years and more and 7 (58.3%) for 1-5 years and for ICD controls 7 (58.3%) were followed up for 5 years or more, 5 (41.7%) for 1-5 years. In both groups (pacemaker and ICD) there were no devices explanted for infection or malfunctioning during the follow up period.

In the re-used pacemaker group, 26 (51%) patients attended follow up at 3 months, whereas 25 (49%) did not attend. Of those who did not attend, 11 (44%) were dead, 9 (36%) were alive and 5 (20%) were lost to follow up (Fig. 2). Of those who died 8 (72.7%) were documented to have died from natural causes, 1 (9.1%) from cancer and 2 (18.2%) from non-pacemaker related sepsis of which one died within 24hours of implantation and the other one after two months of implantation. The patient who died within 24 hours of device implantation was admitted with a methicillin resistant Staphylococcus aureus (MRSA) endocarditis prior to pacemaker implantation.

In the new pacemaker group, 43 (84.3%) patients attended follow up at 3 months, whereas 8 (15.7%) did not attend follow up. Of those who did not attend, 1 (12.5%) was dead and 7 (87.5) were alive (Fig. 2). The patient who died was an 87 year old man who passed away at home two days after pacemaker implantation from natural causes.

At 1year follow up, 19 (37.3%) patients attended follow up, whereas 32 (62.7%) did not attend follow up in the re-used pacemaker group. Of those who did not attend follow up, 15 (46.9%) were dead, 9 (28.1%) were alive and 8 (25%) were lost to follow up (Fig. 2). All deaths were due to natural causes except the two that were septic and mentioned above.

For new pacemaker group, 38 (74.5%) patients attended follow up while 13 (25.5%) patients did not attend follow up at one year. Of those who did not attend follow up, 3 (23.1%) were dead, 7 (53.8%) were alive and 3 (23.1%) were lost to follow up (Fig. 2). All deaths were due to natural causes.

In the ICD group, there was 100% attendance for both cases and controls at 3 months follow up. At 1year follow up there was 100% attendance for cases compared to 91.7% for controls with 1 (8.3%) patient absent but this patient was discharged from Groote Schuur Hospital at 3months of follow up to be followed in Port Elizabeth and is still alive (Fig 2).

Discussion

This study shows that the reuse of pacemakers and ICDs is feasible and safe at Groote Schuur Hospital in Cape Town, South Africa. There was no difference in the incidence of device infection, malfunction, battery failure or explantation due to complications between re-used and new devices. Indeed, device implantation was associated with no complications in this series.

To the best of our knowledge this is the second study ever published of the outcomes of re-used implantable cardioverter defibrillators (ICDs).[25] In our study, there were no device infections and/ or device explanted for malfunction identified. There were no patients that were lost to follow up in this group.

Linde et al.[22] in a retrospective case control study found no significant difference in device infection, although paradoxically more infections were found in the new pacemaker group (7%) than in reused pacemaker group (2%). Kantharia et al.[26] found no significant complications in an Indian study cohort of 53 patients who received cadaveric donated resterilized pacemakers over a mean follow up of 661 days.

Panja et al.[27] found no difference in infection rates between new pacemaker group and cadaver donated re-used pacemakers, but higher rates of infection on infected re-sterilized devices that were implanted on the same patient that were taken out from and implanted on the opposite side. They attributed this higher infection rates to haematogenous or lymphatic spread from previous infected pocket.[27] Rosengarten et al.[28] also found no significant difference in major pacemaker related complications and reported that reuse of devices is cost effective.

Pavri et al.[25] in a retrospective single centre cohort study of re-sterilized ICDs found no device related infections and 60.4% re-used ICDs delivered life-saving shocks. Baman et al.[29] in a meta-analysis of 18 studies found no significant difference in infection rates between new device group and re-used device group but much higher device malfunction associated with re-used devices compared to new devices. This malfunction was attributed to abnormality in set screws.[29] In a recent study, Nava et al.[23] found no significant difference in infection rates between re-used and new devices, although more infections were found in the new device group. They also found more device malfunction in the re-use device group which was similar to the previous quoted studies and also the fault was attributed to faulty pacemaker screws.[23]

Device infection is thought to be associated with mortality rate between 2.6 to 18%.[12-14] There are several factors associated with a greater risk of cardiovascular implantable electronic device infection (1) immunosuppression; (2) oral anticoagulation use; (3) patient coexisting illnesses; (4) peri-procedural factors, including the failure to administer peri-operative antibiotics; (5) device revision/replacement; (6) amount of indwelling hardware; (7) operator experience.[30] However studies that examined this issue showed no significant difference in infection or mortality rates between reused and new device implantation.[14-22]

In our study we did not compare mortality rates between the two groups because of the selection bias of those who received re-used pacemaker.

Although re-used pacemaker patients had more co-morbidities and were expect to have much higher infection rates, we did not find that to be the case in this study. From the findings of this study and also acknowledging its limitations, pacemaker and ICD reuse is feasible and safe, and is a reasonable option for those who cannot afford new devices, provided that proper selection and sterilization measures of re-used devices are followed. In the developing world where there are major resource constraints, this option should be explored for the benefit of those suffering from symptomatic bradyarrhythmias and life threatening tachyarrhythmias.

We acknowledge several limitations of our study. First, this was a retrospective study with small sample size of cases with re-used pacemakers and implantable cardioverter defibrillators. Second, the follow up period of patients with re-used devices was relatively short with a median period of 15 months, with a significant number died within 3 months of device insertion. Finally, the patients who were selected for re-used pacemakers had significant co-morbidities which were associated with a shortned life-span. These factors may limit the generalisability of the study, and call for appropriate prospective studies to answer this question.

Conclusion

Pacemaker and ICD reuse is feasible and safe in the short term (i.e., over months) provided that the devices for reuse are selected carefully and proper sterilization methods are followed. Re-used pacemakers and ICDs are a realistic option for patients with co-morbidities who live in developing countries where there is limited access to pacemaker and ICDs.

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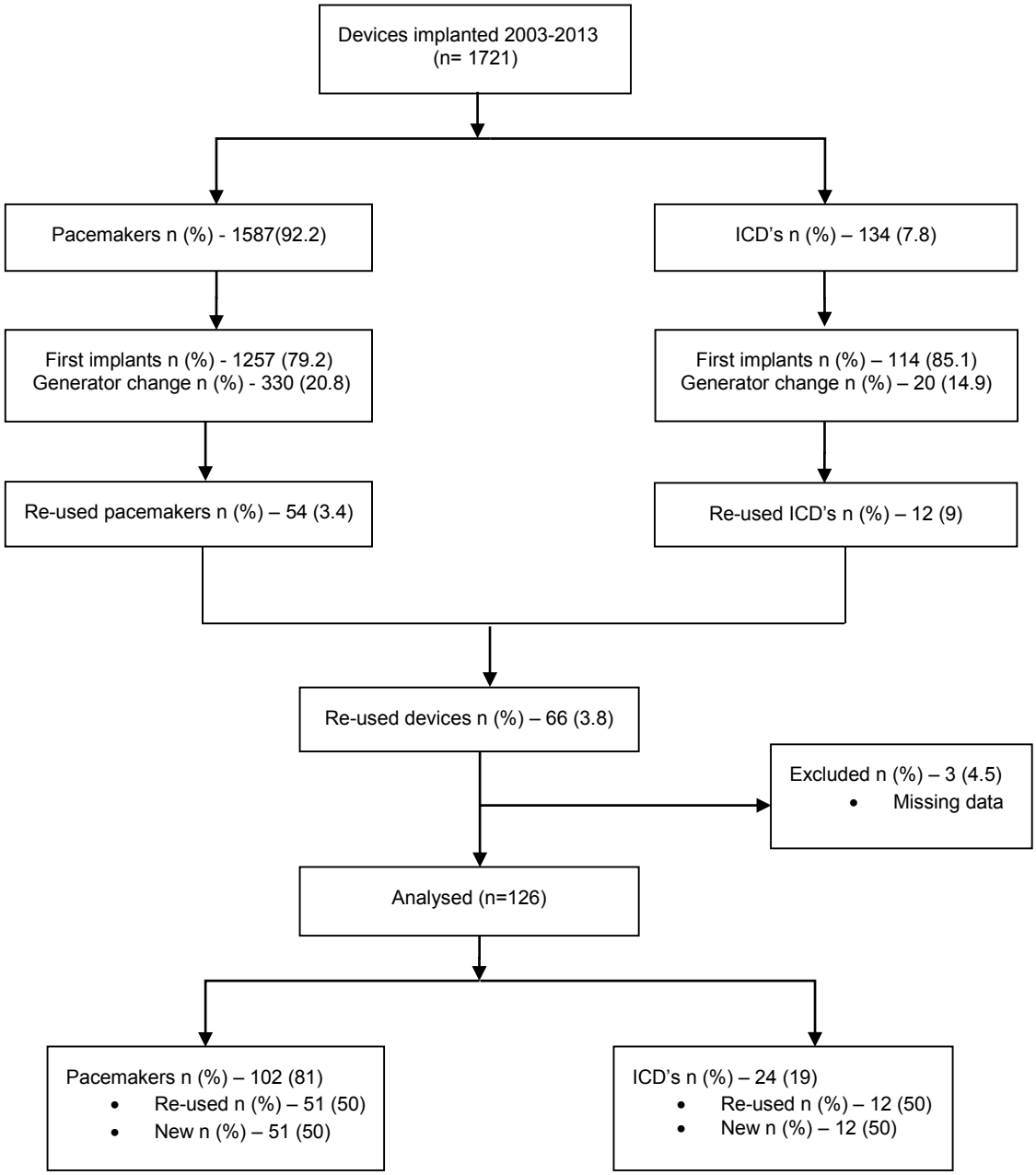
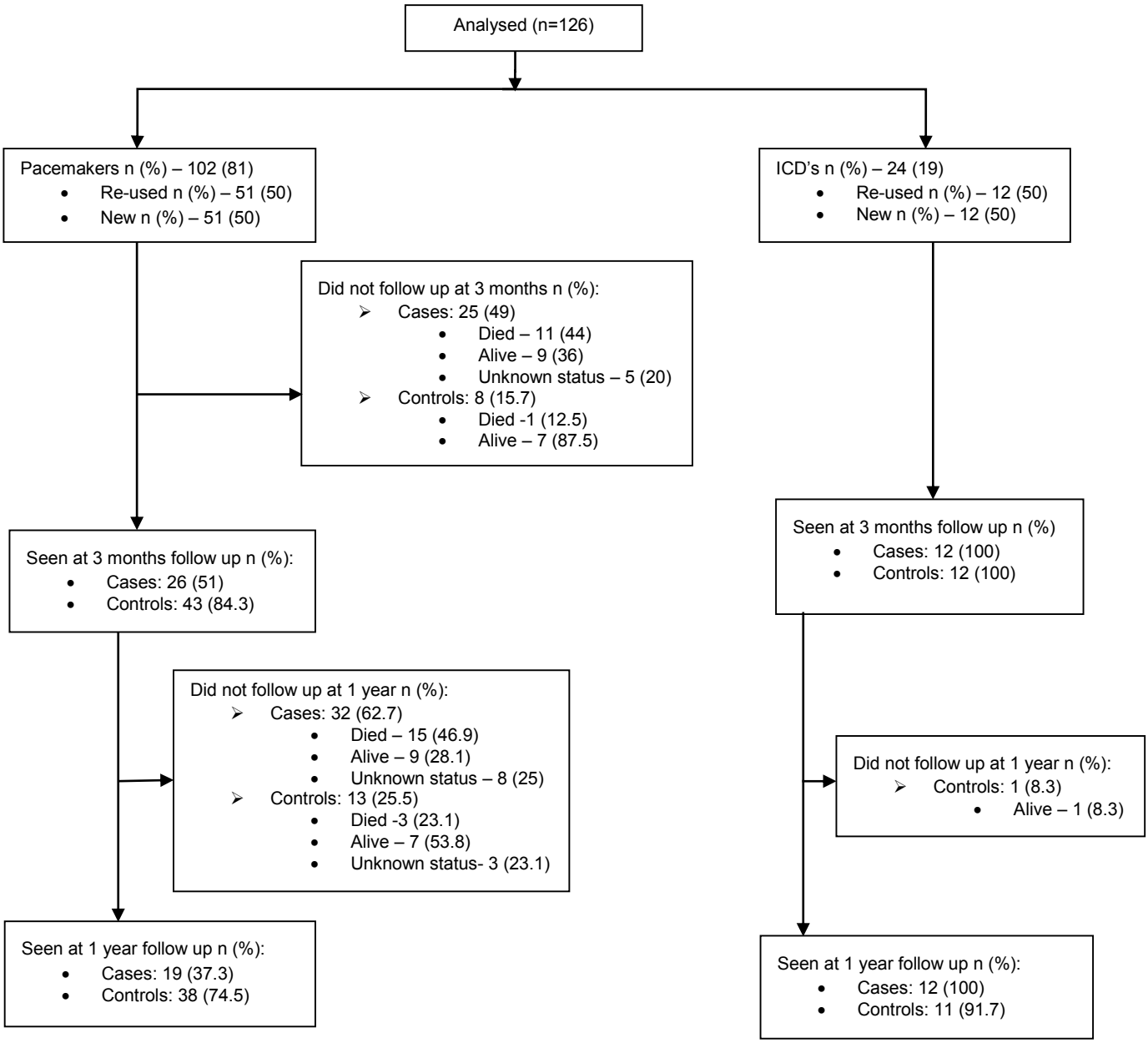
Fig 1: Outline to assess eligibility for enrolment



- ICD's= Implantable Cardioverter-Defibrilators
- n= Number
- (%)= Percentage

Fig 2: Follow up outline



- ICD's= Implantable Cardioverter-Defibrillators
- n= Number
- (%)= Percentage

TABLE 1: Characteristics of patients who received pacemakers

Characteristics	Patients with re-used pacemakers (cases)	Patients with new pacemakers (controls)	P value
Sample size n	51	51	
Age	74.33±17.26	72.86±16.13	0.658
Gender n (%) Male Female	 24 (47.1) 27 (52.9)	 24 (47.1) 27 (52.9)	 1.00
Co-morbidities n (%)			
Hypertension Diabetes mellitus Renal impairment Cancer Myocardial infarction Cardiomyopathy CVA COPD Dementia	26 (51) 7 (13.7) 17 (33.3) 7 (13.7) 6 (11.8) 4 (7.8) 12 (23.5) 5 (9.8) 10 (19.6)	35 (68.6) 13 (25.5) 19 (37.3) 3 (5.9) 11 (21.6) 6 (11.8) 3 (5.9) 1 (2) 1 (2)	0.069 0.135 0.679 0.49 0.29 0.74 0.02 0.21 0.008
Baseline function n (%)			
NYHA Functional Class 1 NYHA Functional Class 2 NYHA Functional Class 3 Wheelchair bound Bed bound	3 (5.9) 15 (29.5) 14 (27.5) 4 (7.8) 15 (29.4)	7 (13.7) 27 (52.9) 14 (27.5) 3 (5.9) 0 (0)	0.32 0.026 1.00 1.00 <0.0001
Indication			
Sick sinus syndrome n (%)			0.138
Yes	9 (17.6)	4 (7.8)	
No	42 (82.4)	47 (92.2)	
AV block n (%)			0.22
Yes	38 (74.5)	43 (84.3)	
No	13 (25.5)	8 (15.7)	
Others n (%)			1.00
Yes	4 (7.8)	4 (7.8)	
No	47 (92.2)	47 (92.2)	
First implantation n (%)	43 (84.3)	45 (88.2)	0.565
Generator change n (%)	8 (15.7)	6 (11.8)	0.565
Primary implanter Cardiologist Cardiology registrar	 25 26	 25 26	 1.00 1.00
Temporal lead n (%)	17 (33.3)	21 (41.2)	0.413
Follow up @ 3/12 n (%) YES NO	 26 (51) 25 (49)	 43 (84.3) 8 (15.7)	 <0.0001
Follow up @ 1YR n (%) YES NO	 19 (37.3) 32 (62.7)	 38 (74.5) 13 (25.5)	 <0.0001

CVA= Cerebrovascular Accident; COPD= Chronic Obstructive Pulmonary Disease; NYHA= New York Heart Association; AV Block= Atrioventricular Block; n= Number; (%) = Percentage; 3/12= 3 months; YR= Year; Other= atrial fibrillation and heart failure.

TABLE 2: Pacemaker parameters

Parameters	Patients with re-used pacemakers (cases)	Patients with new pacemakers (controls)	P value
DDD n (%)	11 (21.6)	7 (13.7)	0.30
VVI n (%)	39 (76.5)	42 (82.4)	0.463
Others n (%)	1 (2)	2(3.95)	
Minimum pacing rate,bpm	63.4±6.0	61.6±5.1	0.09
Ventricular pacing %	50 (98%)	49 (96.1)	0.558
Battery voltage, V	2.78 (2.77-2.79)		
Battery current, A	13.86±4.9		
Battery impedance, KΩ	0.482±0.3		
Estimated battery life	6.085±1.7		
Capture			
Amplitude, V Atrial Ventricular	 0.48±0.15 0.49±0.34	 0.57±0.23 0.48±0.18	 0.323 0.747
Pulse width, ms Atrial Ventricular	 0.5 (0.5-0.5) 0.5 (0.5-0.5)	 0.5 (0.475-0.5) 0.5 (0.5-0.5)	 0.485 0.355
Sensitivity, mV Atrial Ventricular	 4.3 (3.750-5.5) 14.09±6.50	 3.8 (2.875-6.2) 15.27±7.14	 0.255 0.406
Electrode impedance Ω Atrial Ventricular	 692±178 748±267	 804±275 808±285	 0.289 0.289

Others= AAI, V= volts; mV= millivolts; ms= milliseconds; Ω= ohms; KΩ= kilohms; A=amperes; bpm= beats per minute; DDD= dual chamber pacemaker; VVI= single chamber pacemaker

TABLE 3: Characteristics of patients who received implantable cardioverter-defibrillators

Characteristics	Patients with re-used ICDs (cases)	Patients with new ICDs (controls)	P value
Sample size n	12	12	
Age	49.83±17.34	50.58±17.27	0.916
Gender n (%) Male Female	 10 (83.3) 2 (16.7)	 10 (83.3) 2 (16.7)	
Co-morbidities n (%)			
Hypertension Diabetes mellitus Renal impairment Cancer Myocardial infarction Cardiomyopathy CVA COPD Dementia	4(33.3) 1 (8.3) 8 (66.7) 0 (0) 7 (58.3) 3 (25) 1 (8.3) 2 (1.7) 0 (0)	4 (33) 2 (16.7) 6 (50) 0 (0) 4 (33.3) 2 (1.7) 1 (8.3) 0 (0) 0 (0)	1.00 0.537 0.408 0.49 1.00 1.00 0.48
Baseline function n (%)			
NYHA Functional Class 1 NYHA Functional Class 2 NYHA Functional Class 3 Wheelchair bound Bed bound	1 (8.3) 7 (58.3) 4 (33.3) 0 (0) 0 (0)	5 (41.7) 7 (58.3) 0 (0) 0 (0) 0 (0)	0.20 1.00 0.11
Ventricular Tachycardia n (%)	9 (75)	10 (83.3)	0.615
Others n (%)	3 (25)	2 (16.7)	0.615
First implantation n (%)	12(100)	11(91.7)	0.307
Generator change n (%)	0(0)	1 (8.3)	0.307
Primary implanter n (%) Cardiologist Cardiology registrar	 11 (91.7) 1 (8.3)	 12 (100) 0 (0)	 1.00
Follow up @ 3/12 n (%) YES NO	 12 (100) 0 (0)	 12 (100) 0 (0)	 1.00
Follow up @ 1YR n (%) YES NO	 12 (100) 0 (0)	 11 (91.7) 1 (8.3)	 0.307

CVA= Cerebrovascular Accident; COPD= Chronic Obstructive Pulmonary Disease; NYHA= New York Heart Association; AV Block= Atrioventricular Block; n= Number; (%) = Percentage; 3/12= 3 months; YR= Year; Others= ventricular fibrillation and arrhythmogenic right ventricular cardiomyopathy.

TABLE 4: Implantable cardioverter-defibrillator parameters

Parameters	Patients with re-used ICDs (cases)	Patients with new ICDs (controls)	P value
VVI n (%)	12	12	1.00
Minimum pacing rate,bpm	38.1±4.7	44.4±9.4	0.052
Ventricular pacing %	12	12	1.00
Capture			
Amplitude, V Ventricular	0.618±0,28	0.708±0.32	0.481
Sensitivity, mV Ventricular	12.925±6.93	16.118±6.17	0.258
Output			
Amplitude, V Ventricular	3.5 (3.3-3.875)	3.5 (3-3.5)	0.875
Electrode impedance Ω Ventricular	784.75±304	648.83±147	0.177

V= volts; mV= millivolts; ms= milliseconds; Ω= ohms; KΩ= kilohms; A=amperes; bpm= beats per minute; VVI= single chamber device

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I would like to dedicate this work to the late Professor Andrzej Okreglicki, who believed in this practice and today made it possible for me to conduct such a study in Groote Schuur Hospital.

I thank you

Regards

Zimasa V. Jama

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28 October 2013

HREC REF: 639/2013

Dr Z Jama
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OMB

Dear Dr Jama

PROJECT TITLE: OUTCOMES RE-STERILISED PACEMAKERS AND IMPLANTABLE CARDIOVERTER DEFIBRILLATORS (ICD's) IN COMPARISON WITH NEW DEVICES IN GROOTE SCHUUR HOSPITAL

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee for review.

It is a pleasure to inform you that the HREC has formally approved the above-mentioned study.

Approval is granted for one year until the 30th October 2014

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period. (Forms can be found on our website: www.health.uct.ac.za/research/humanethics/forms)

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the HREC reference no in all your correspondence.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN ETHICS
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938
This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP) and Declaration of Helsinki guidelines.
The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

Please note that the title that you see on the ethics approval letter has slightly changed to the current title of this thesis and the application for title change has been submitted and was approved in March 2015.