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Years of life lost as a measure of premature death among inhabitants of Malopolska Province implanted with dual-chamber pacemaker

Brief title: YLL in patients with dual-chamber pacemaker

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What is new?

In this paper we investigated the lifespan of DDD pacemaker recipients who were inhabitants of Malopolska Province. We performed a trend analysis of age at implantation, survival after implantation and age at death between 1999 and 2015. Furthermore, we evaluated premature mortality measured with years of life lost method over a 17-year period. The results demonstrated continuous improvement in the survival after DDD pacemaker implantation and significant reduction of years of life lost. To our knowledge, it is the first report adopting an accurate and comprehensive measure which quantifies the level and trend of premature mortality in patients with permanent pacemaker.
Abstract:

**Background**: Pacemakers have become the standard of care for patients with severe bradycardia and conduction abnormalities. The survival prolongation and premature mortality can be assessed using Years of Life Lost (YLL).

**Aims**: To analyse mortality trends over the period 1999-2015 among inhabitants of Malopolska Province implanted with DDD pacemaker.

**Methods**: Retrospectively collected records comprised all consecutive patients who underwent de novo DDD pacemaker implantation at single-centre between 1984-2014. Inclusion criteria included Malopolska Province inhabitant status at latest follow-up visit and death between 1999 and 2015. Standard Expected Years of Life Lost per death was used to calculate YLL. Time trends were evaluated with joinpoint models and presented as average annual percentage change (AAPC).

**Results**: Among a total of 3932 consecutive patients implanted with DDD pacemaker 1211 patients met study inclusion criteria. We noted an increase in mean age at implant from 70 in 1999 to 75.5 in 2015 (AAPC 0.6%; p < 0.05), the number of years lived after DDD pacemaker implantation from 2.6 years to 8.2 years (AAPC 7.4%; p < 0.05) and the mean age at death from 72.6 to 83.8 (AAPC 0.89%; p < 0.05). Finally, we observed the reduction of YLL per death from 17.4 in 1999 to 9 years in 2015 (AAPC -4%; p < 0.05). All trends were significant for both men and women.

**Conclusions**: In the 17-year-long period we showed statistically significant changes in analysed trends, in particular a reduction in years of life lost per death.

**Key words**: average annual percentage change; pacemaker; premature mortality; years of life lost
Introduction:
As shown in the FOLLOWPACE study published by Udo et al. pacemakers implanted for slow heart rhythm restore life expectancy to normal levels. [1] The results have suggested that the prognosis of contemporary pacemaker patient was primarily determined by concomitant cardiovascular disease, and not by the rhythm disorder itself. Therefore, after pacemaker implantation for bradycardia, more attention should be paid to the detection and treatment of other concurrent cardiovascular conditions. Noteworthy, in the previous study we showed that compared to the general population the observed survival of dual-chamber (DDD) pacemaker recipients was significantly inferior until 12 years post implant, whilst after 12 years of follow-up the observed survival was significantly superior. [2] Death rates alone do not provide a complete picture of the burden that deaths impose on the population. Another useful measure which has been gaining an increasing popularity in epidemiological reports is years of life lost indicator. This less conventional indicator may add a different dimension to mortality trends in population, in particular with regard to premature mortality. According to Eurostat, Years of Life Lost (YLL) is the mortality component of the DALY (disability adjusted life years), introduced by the World Bank and the WHO as a description of the ‘burden of disease’. YLL ignores morbidity, and therefore only describes ‘the burden of mortality’. [3] The aim of the study was to analyse mortality trends in the period 1999-2015 among inhabitants of Malopolska Province implanted with DDD pacemaker using YLL measure.

Methods:
Retrospectively collected records comprised all consecutive patients who underwent primary DDD pacemaker implantation at a high-volume, tertiary reference university implantation centre between 4th October 1984 and 31st December 2014. Detailed methods of data collection and population baseline characteristics were presented previously. [2,4] The study
inclusion criteria were the Malopolska Province inhabitant status at the time of last pacemaker follow-up visit and death between 1st January 1999 and 31st December 2015. Malopolska Province came into being on 1st January 1999. The data of patients’ survival status and deceased patients’ dates of death were collected from the national death registration system in 2016. The data used in the analysis included (1) patients’ demographic baseline characteristics: date of birth, age at implantation, sex; (2) place of residence during follow-up; (3) date of death declared in the death certificate. Following time trends were analysed: (1) YLL per one death; (2) mean age at the time of death; (3) mean age at implantation; (4) mean time from implantation to death.

Statistical analysis

Time trends of analysed variables were evaluated using Joinpoint Regression software developed by U.S. National Cancer Institute for the Surveillance, Epidemiology and End Results Program (Joinpoint Regression Program, Version 4.1.1.1. October 2014; Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Institute, Bethesda, MD, USA, 2014). This method is an advanced version of linear regression, where the time trend is expressed with a broken line, which is a sequence of segments joined in Joinpoint. To confirm whether the changes were statistically significant, the Monte Carlo Permutation method was applied. We estimated the annual percentage change (APC) of the variables for each segment of the segmented regression curve, average annual percentage change (AAPC) as a summary measure of trend that applies over an entire time period, and their 95% confidence intervals. When the trend is constant over the entire period of the interest the AAPC will be equal to the estimated APC. [5] In all analyses, p < 0.05 was considered statistically significant.
To calculate years of life lost (YLL) the authors used the Standard Expected Years of Life Lost per death (SEYLL) measure. SEYLL was used to calculate the number of years of life lost by the studied population in comparison to the years of life lost by the standard population. SEYLL weighs mortality, age at death, the population structure, counts all life years lost at all ages, and weighs death by the residual life expectancy in a standard life table.

In the present study SEYLL index was calculated according to Marshall Method and expressed as a rate per a single death. [6]

\[
\text{SEYLL} = \sum_{a=0}^{k} d_a e_a
\]

\(a\) – age at death,
\(k\) – age of the oldest deceased patient,
\(d_a\) – number of patients deceased at the age of \(a\),
\(e_a\) – number of expected years of life for a person at the age of \(a\),

The expected number of years of life \(e_a\) for a person at the age of \(a\) was calculated based on standard life table presented by Murray et al. in Global Burden of Disease Study 2010. [7]

Results

A total of 3932 consecutive patients underwent primary DDD PPM implantation from 1984 to 2014, 53.7% were male. The data of patients’ survival status were available for 3928 patients (99.9%). At the time of the last follow-up appointment 3702 (94.2%) patients were inhabitants of Malopolska Province. Among inhabitants of Malopolska Province 1211 patients died between 1999-2015, 696 (57.5%) men and 515 (42.5%) women (Table 1). In other provinces there were 69 deaths. During follow-up out of 1211 patients seven had device upgrade to implantable cardioverter defibrillator, eight had an upgrade to cardiac resynchronisation therapy pacemaker (CRT-P) and three had an upgrade to cardiac
resynchronisation therapy defibrillator (CRT-D). We observed the increase in mean age at the time of implantation from 70 in 1999 to 75.5 in 2015 with AAPC of 0.62% (95% CI, 0.4% to 0.9%; p < 0.05); in women from 75.2 to 76.7 with AAPC of 0.29% (95% CI, 0.1% to 0.5%; p < 0.05) and in men from 68.6 to 74.2 with AAPC of 0.72% (95% CI, 0.4% to 1%; p < 0.05) (Figure 1). In the analysed time period from 1999 to 2015 we observed prolonged life span after primary DDD PPM implantation, for both women and men. In 1999 the survival after pacemaker implantation amounted to 2.6 years (in women 2.4 years and in men 2.7 years), whereas in 2015 reached 8.2 years (in women 7.3 years and in men 9.3 years). The average rise in the number of survived years after PPM insertion calculated as AAPC amounted to 7.4% (95% CI, 4.2% to 10.7%; p < 0.05) in the whole study group; 8.2% (95% CI, 5% to 11.5%; p < 0.05) in women and 6.3% (95% CI, 1.7% to 11.1%; p < 0.05) in men. Among women who died between 1999 and 2003 and men who died between 1999 and 2001 the APC of post-implant survival reached 34.2% (95% CI, 19.4% to 50.8%; p < 0.05) and 34.3% (95% CI, -7.7% to 95.5%; p > 0.05), respectively. In the later period, for women who died between 2004 and 2015 and for men who died between 2002 and 2015 the APC was lower and amounted to 0.7% (95% CI, -1.4% to 3%; p > 0.05) and 2.8% (95% CI, 1% to 4.6%; p < 0.05), respectively (Figure 2). Furthermore, the mean age at the time of death was increasing at the rate of 0.9% (95% CI, 0.7% to 1%; p < 0.05); 0.6% (95% CI, 0.4% to 0.8%; p < 0.05) for women and 1% (95% CI, 0.6% to 1%; p < 0.05) for men. The mean age of deceased pacemaker recipients in 1999 was 72.6 (in women 77.6 and in men 71.2), whereas in 2015 it was 83.8 (in women 84 and in men 83.5) (Figure 3). Finally, we observed the decrease of YLL per death with AAPC of -4% (95% CI, -4.9% to -3.1%; p < 0.05); -2.9% (95% CI, -3.9% to -2%; p < 0.05) for women and -4.2% (95% CI, -5.2% to -3.1%; p < 0.05) for men. YLL per death in 1999 amounted to 17.4 (in women 13.3 and in men 18.6), whereas in 2015 YLL per death dropped to 9 (in women 8.8 and in men 9.2) (Figure 4).
Discussion

In this paper, we demonstrate trends in DDD pacemaker recipients’ characteristics and outcomes among Malopolska Province patients in Poland across a 17-year period from 1999 to 2015. We observed shifts toward DDD pacemaker implantation in older age, extended longevity after primary implant, and reduction in years of life lost per death. Furthermore, we noted that among men the APC of YLL reduction was greater than in women. Our findings provide robust evidence for trends in demographics and survival among large group of DDD pacemaker recipients.

Few studies have investigated the epidemiology of patients with dual-chamber pacing. Our previously presented findings demonstrated that women were older than men at the time of pacemaker implantation and showed the rise in average age at implant across the three decades. Similar trends have been observed in other countries [2,8-13]. In the present study we found that the average trend of increasing age at implantation in men exceeded the trend observed in women, which has not been previously reported. The significantly extending life expectancy of pacemaker recipients being implanted in the consecutive decades was shown by Brunner et al. [9] On the contrary, Bradshaw et al. concluded that era of implantation was not an independent predictor of mortality after adjustment for age. [8] Several authors have argued that the prognosis of pacemaker recipients did not differ compared to general population unless significant comorbidities were present. [1,8,14,15] Of note, our findings show consistently extending life expectancy after the implantation despite gradually increasing age of pacemaker recipients. To appreciate it fully we may need to look at it in the broad context of economic, cultural and behavioural changes reflecting Poland’s progress between 1999 and 2015. The study by Global Burden of Disease 2017 sheds light on global and regional changes in mortality between 1980 and 2017 [16]. In general, YLL rates decreased as socio-demographic index for a given region increased. Non-communicable
diseases, including both cardiovascular diseases and neoplasms, have risen steadily since 1990 in terms of total number of deaths, driven by ageing and population growth, while death rates and YLL rates have been falling consistently, as a result of improvements in prevention strategies and health-care. In Poland the observed life expectancy between 2000 and 2017 rose from 78 to 81.8 years for women and from 69.6 to 74.1 years for men. [17] Non-communicable diseases contributed to 76.9% of years of life lost among males and 87.5% years of life lost among females in 2000. [18] The total all-cause mortality rate for age group at 70 and above in 1999 was 7,273 deaths per 100,000 and in 2015 it dropped to 6,361 deaths per 100,000. The rate of deaths attributable to cardiovascular diseases in this population decreased from 4,226 deaths per 100,000 in 1999 to 3,215 deaths per 100,000 in 2015. Between 2000 and 2014, the rates of the YLL per death due to cardiovascular diseases dropped with AAPC -0.5% among males and -1.4% among females. [19] In the present study the pace of decline in YLL per death was significantly higher with AAPC of -4.2% among men and AAPC of -2.9% for women across the 17-year study period. This remarkable difference may be explained by the close, mostly life-long follow-up of pacemaker recipients by highly specialised cardiologists in a tertiary reference centre which provides comprehensive cardiology and cardiothoracic care and access to other medical and surgical facilities. Interestingly, the observed statistically significant rise in the lifespan after implant in women between 1999 and 2003 with APC over 34% corresponds to a significant drop in SEYLL per living person due to chronic non-communicable diseases among inhabitants of Poland in the period 2000-2003. [18] The trend for men in the period 1999-2001 was not statistically significant, most likely due to the small sample. Since 1990 the two leading causes of death in Poland have continued to be ischemic heart disease and stroke. Noteworthy, rate of YLL per death secondary to ischemic heart disease decreased statistically significantly in 2000-2014 with AAPC of -1% for men and -1.2% for women and secondary
to cerebrovascular diseases at the pace of -0.5% for men and -1.3% for women. [19] On balance, the number of YLL has increased for lung cancer, colorectal cancer and Alzheimer’s disease. Importantly, according to GBD the Healthcare Access and Quality Index in Poland has been improving between 2000 and 2016 with AAPC of 0.9%, which was statistically significant. This measure is based on risk-standardized mortality rates or mortality-to-incidence ratios from causes that, in the presence of quality healthcare, should not result in death – also known as amenable mortality. Additionally, the behavioural/metabolic/occupational risk changes in Poland between 2007 and 2017 have resulted in less deaths and disability due to tobacco, dietary risks, hypertension and hypercholesterolemia, whereas high body-mass index and high fasting plasma glucose have contributed to more deaths and disability.

Study limitations

Our findings should be interpreted in the context of limitations imposed by a retrospective study design. Due to the lack of cause for death we were unable to perform comparisons with general population. Moreover, the results cannot be generalised for general pacemaker population as our sample consisted of only DDD pacemaker recipients. In addition, the present study population consisted of patients who deceased and were inhabitants of Malopolska Province at the last follow-up and excluded patients who remained alive until 2015 or were inhabitants of other provinces. On the other hand, the life expectancy may vary across regions in Poland and therefore by narrowing the sample we aimed to obtain the most accurate estimation of patients’ demographics and lifespan. Nonetheless, we believe that the ability to generate locally representative estimates of demographic and survival trends in DDD pacemaker population is the strength of our study.

Conclusions:
In summary, we identified a shift toward favourable life expectancy and decrease in years of life lost among DDD recipients in Polish Malopolska Province. Many of the factors driving that positive trend include state-of-the-art cardiology care during follow-up but also national economic transformation, improvement in general health-care system and behavioural and lifestyle changes.

References:


Table 1 Number of patients meeting study inclusion criteria.

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Figure 1 Age at the time of primary DDD pacemaker implantation

Figure 2 Average lifespan following DDD implant
Figure 3 Average age at the time of death

Figure 4 Years of life lost per death