

Long-term follow-up of patients undergoing permanent pacemaker implantation: GATA experience

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ÖZET

KALICI PACEMAKER YERLEŞTİRİLEN HASTALARIN UZUN DÖNEM TAKİBİ: GATA DENEYİMİ

Amaç: Kalıcı pacemakerlar birçok hastalığın tedavisinde hayati öneme sahiptir. Tek odacıklı (özellikle ventriküler) ve çift odacıklı leadlere sahip olmak üzere iki farklı seçenek bu hastalıkların tedavisinde kullanılabilir. Ventriküler pacemakerlar daha ucuzdur, ancak iki odacıklı pacemakerların daha fizyolojik olduğu bilinmektedir. Bu çalışmada hastalarda uzun dönem kardiyovasküler mortaliteyi karşılaştırmayı amaçladık.

Gereç ve Yöntemler: Bu tek merkezli retrospektif çalışmada Ocak 1994 ve Aralık 2013 tarihleri arasında VVI ya da DDD pacemaker takılan 240 ardışık hasta incelendi.

Sonuçlar: Toplam 29 hasta VVI ve 211 hasta ise DDD pacemaker implantasyonuna gitti. Ortanca takip süresi 44,1 aydı (21.6-90.3). Takip süresince 41 (%17,1) hasta kaybedildi. VVI pacemaker implante edilen grupta 13 hasta takip sırasında kaybedildi. DDD grubunda ise 28 hasta kaybedildi. DDD pacemaker implante edilen hastalarda VVI pacemaker implante edilenlere göre gözlemlenen kardiyovasküler nedenlere bağlı yıllık ölüm oranları daha azdı (Fizyolojik pace grubunda %7,3'e karşılık ventriküler pace grubunda %1,5).

Sonuç: Kalıcı pacemaker implantasyonu sağlıklı yaşam süresini arttırmaktadır. VVI ve DDD pacemaker karşılaştırıldığında DDD pacemakerlardaki hayat süresi artışı daha çok sinus nod disfonksiyonu olan hastalarda gözlemlenmektedir.

Anahtar Kelimeler: Uzun dönem mortalite, DDD pacemaker, VVI pacemaker

SUMMARY

Objective: Permanent pacemaker implantation is an essential in many cardiovascular disorders. In present, one lead pacemaker implantation (especially ventricular) and dual-chamber pacemakers may be used to treat these disorders. Ventricular pacemaker implantation is less expensive, but dual-chamber pacemakers are known to be more physiologic. In that study, we aimed to compare long-term cardiovascular mortality in those patients.

Material and methods: Between January 1994 and December 2013, 240 consecutive patients implanted VVI or DDD pacemakers (PM)s were examined in this retrospective single-centre study.

Results: A total of 29 patients underwent VVI PM and 211 underwent DDD PM implantation. The median follow-up duration was 44.1 months (21.6-90.3). Forty one (17.1%) patients died during the follow-up period. Among the 29 patients implanted with a VVI, 13 died during follow-up. In the DDD group, 28 deaths were recorded. The observed annual rates of death from cardiovascular causes were lower in the patients undergoing DDD PM compared to that of the patients undergoing VVI PM (annual rates of death, 1.5 percent with ventricular pacing and 7.3 percent with physiologic pacing, respectively).

Conclusion: The implantation of permanent pacemaker decreases the mortality rate. When comparing VVI and DDD pacing, the mortality rate is lower the dual-chamber pacing as compared with ventricular pacing are observed principally in the subgroup of patients with sinus-node dysfunction.

Key words: Long-term mortality, DDD pacemaker, VVI pacemaker

Introduction

Cardiac pacemakers (PMs) are widely recognized as beneficial in the treatment of various types of electromechanical abnormal conditions. Today, more than 40 years after the first pacemaker implantation, world-wide implantation rate exceeds 400000 every year(1). Standard clinical practice permits the use of either single-chamber ventricular pacemakers or dual-chamber pacemakers for most patients who require cardiac pacing(2). In a single-chamber system, one lead is used, they may be atrial or ventricular, most commonly pacing the right ventricle except for only sinus node disease. Dual-chamber pacemakers have two leads, placed in the right atrium and right ventricle. They act synchronously when a slow natural heart rate is detected to mimic the sequential physiological contraction of the atria and ventricles. Atrial pacemakers are used where slow heart rate is due only to sinoatrial disease, i.e. where conduction between the atria and ventricles is intact. Single-chamber ventricular pacemakers, which are much more commonly used in practice, are appropriate where conduction between the atria and ventricles is impaired(3). In order to clarify advantages and disadvantages of each pacing mode, we compared long-term survival of our patient who received atrial synchronous (DDD) and activity rate modulated ventricular (VVI) PMs.

Methods

Between January 1994 and December 2013, 240 consecutive patients implanted VVI or DDD PMs as primary implantation for symptomatic atrioventricular (AV) conduction and sinoatrial disorders were included in this retrospective single-centre registry. Pacemaker implantation and patient follow-up took place in our centre. Assignment to VVI or DDD pacing was dependent on the choice of the physician. The present study was conducted in accordance with the Declaration of Helsinki. The patients who have missing data were excluded.

Clinical follow-up and pacemaker control

Patients were followed up every 6 months by a rythmologist. Visits included clinical examination, recording of a 12-lead ECG and PM interrogation. Atrial and ventricular pacing and sensing thresholds, AV sensing, and pacing interaction were collected. An atrial sensing threshold of<0.5 mV was considered as poor. Patients with atrial undersensing were monitored after adaptation of the atrial sensitivity to ensure optimal AV synchrony. Standard antero-posterior and lateral chest X-ray was performed at 24 h and 2 months post-implantation and when poor atrial sensing or AV dissociation was discovered on regular 6-monthly PM control. Exercise stress test and 24 h Holter monitoring were also recorded if the patient's clinical

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cal situation warranted it. The former was performed to show evidence of AV dissociation on exertion in patients experiencing exertional dyspnoea, the latter, to evaluate sinus node function and presence of arrhythmia in patients complaining of palpitations. The incidence of atrial arrhythmias was also assessed through analysis of the PM control. Only patient with permanent AV dissociation and/or PM syndrome were considered for upgrading of their PM. At least, one transthoracic echocardiography was performed over the follow-up period. Left ventricular (LV) function was measured.

Between 1 January 2014 and 31 March 2014, all patients were called back to undergo a final control visit which included a full medical examination, recording of a 12-lead ECG and PM interrogation and check, a standard antero-posterior and lateral chest X-ray, and a final transthoracic echocardiography. In the case of death or loss to follow-up, patients' data were gathered from their last visit records.

Outcome events

Death and specified cardiovascular events were collected. Cardiovascular death was defined as sudden death, cardiogenic shock (whether from coronary heart disease or not), terminal heart failure, or fatal stroke. Myocardial infarction and dilated cardiomyopathy were also collected. If the follow-up visit was missed, outcome data were sought through a review of clinical records or through contact with the patient, his family, or the patient's family doctor.

Statistical Analysis

Statistical analyses were performed by using SPSS 15.0 Statistical Package Program for Windows (SPSS Inc., Chicago, Illinois, USA). Continuous variables were compared using a two-tailed student's t-test. Categorical variables were compared using the Fisher's χ^2 test. Data are presented as mean with standard deviations. The level of significance was determined by a P value < 0.05 . Overall survival functions were analysed using Kaplan–Meier

Curves and compared using the log rank statistics. All clinical variables were submitted to a univariate analysis. Variables which correlated to survival with a P value < 0.10 were subsequently. Differences were considered significant at $p < 0.05$ two-sided.

Results

Patient population

Three hundred and fifty five patients underwent PM implantation between January 1994 and December 2013. A total of 240 patients were included in the study of whom 29 (12.1%) received a VVI PM and 211 (87.9%) received a DDD PM. Pacing indications were third-degree or second-degree AV block in 135 (56.2%), sinus node dysfunction (SND) in 93 (38.8%) and carotid sinus syncope or vasovagal syncope in 12 (5.0%). At inclusion, there was no significant difference in the use of aspirin, angiotensin-converting-enzyme-inhibitor, angiotensin II-receptor antagonists, diuretic, nitrate or other vasodilator, beta-blocker, lipid-lowering agent in the two groups.

Clinical follow-up and pacemaker control

The median follow-up duration was 44.1 months (21.6–90.3). Forty one (17.1%) patients died during the follow-up period. Among the 29 patients implanted with a VVI, 13 died during

follow-up. In the DDD group, 28 deaths were recorded.

Long-term outcome

We compared these patients long-term mortality in respect to some conditions. Firstly, significant differences were seen in the survival of patients during the decades (Figure 1). The Kaplan–Meier survival graphs were stopped at 75 months due to the number of patient at risk after this time limit (23 in the VDD group and 15 in the DDD group). We have also analyzed the survival of patients after pacemaker implantation according to electrocardiographic indication. CSS or VVS group was significantly higher overall survival compared the other indications (Figure 2). In another, we also compared the survival of patients after pacemaker implantation according to pacing mode. At the end of the follow-up period, the overall survival was significantly lower in the VVI group compared with the DDD group, (Figure 3, 4).

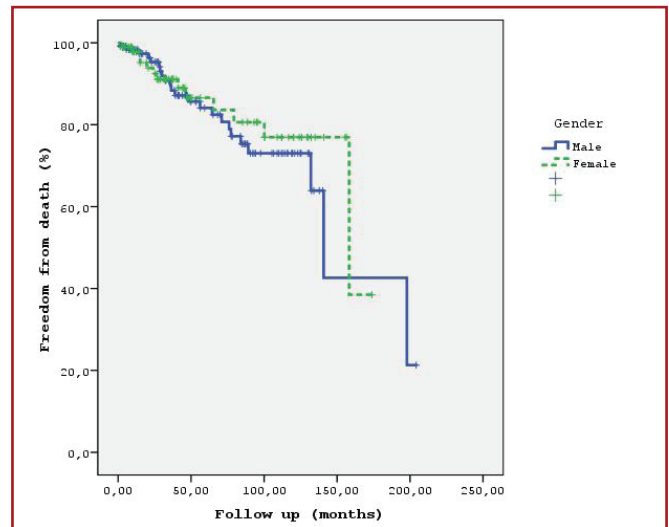


Figure 1. Kaplan-Meier analysis of survival of patients after pacemaker implantation according to gender.

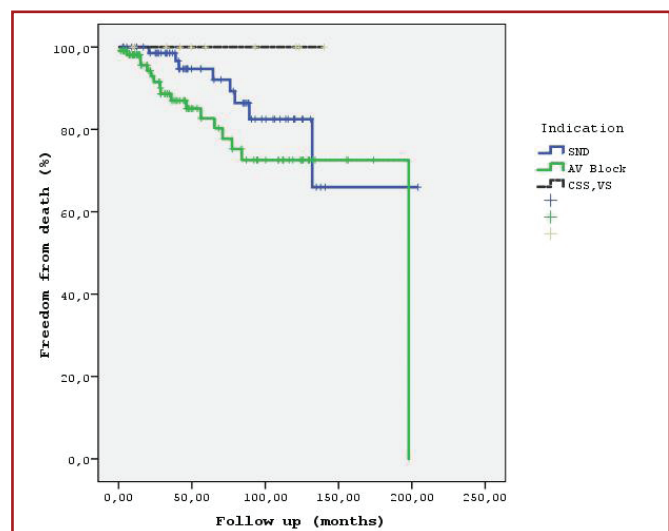


Figure 2. Kaplan-Meier analysis of survival of patients after pacemaker implantation according to electrocardiographic indication.

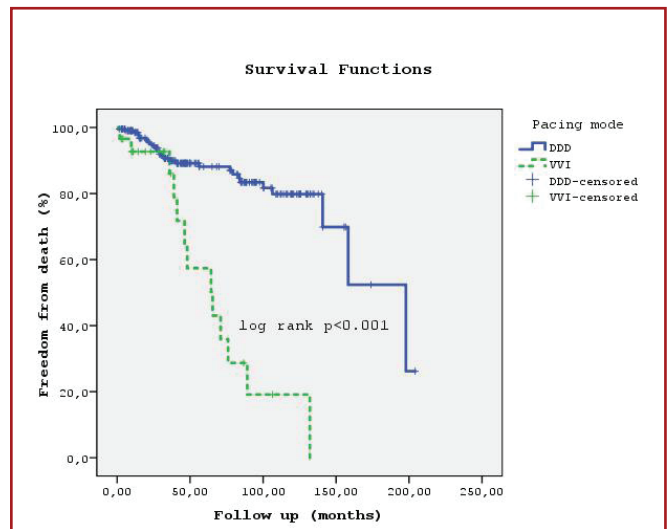
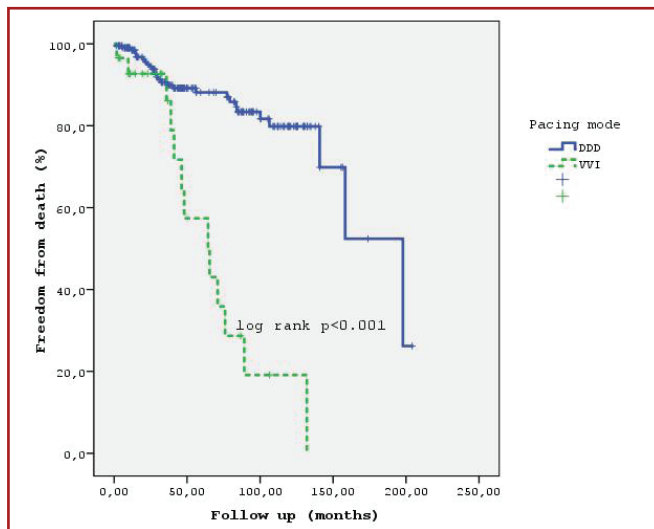


Figure 3 and 4. Kaplan-Meier analysis of survival of patients after pacemaker implantation according to pacing mode.

Discussion

Permanent pacemaker therapy has established as one of the most effective forms of cardiological therapy for the indications like AV-block, SND, bradyarrhythmia, and carotid sinus syndrome. PM technology and clinical practice permit the use of either VVI or DDD for patients who require cardiac pacing. In current guidelines, single lead VVI PMs are an alternative to DDD PMs in patients with AV conduction block(4). In the present study, we have showed that not only DDD pace maker therapy but also VVI pace maker therapy is beneficial effect for above indications.

Single lead pacemakers are less expensive, are easier to implant, and have longer service lives than dual-chamber pacemakers and they present the advantages of reducing procedure time, complications, and cost, they avoid the problems of atrial lead function abnormalities (2). A potential disadvantage of VVI pacing is the possible increased incidence of the development of atrial fibrillation with its attendant risk of thromboembolism. In comparison of single-chamber PMs, dual-chamber PMs can sense the activity of, and pace, both the atrium and the ventricle and thus are able to achieve atrioventricular synchrony (physiologic pacing). This physiologic pacing resembles cardiac physiology more likely by maintaining AV synchrony and dominance of the sinus node, that in turn may decrease cardiovascular morbidity and mortality thus contributing to patient survival and quality of life(4). With widespread use, pacemaker technology has greatly evolved, and highly sophisticated devices have become available providing optimal support for treating any type of bradyarrhythmia. However, in a previous study, the authors concluded that for most patients with high degree AV block, DDD and VVI pacing seem equally satisfactory for submaximal exercise(5). The results of several nonrandomized, observational studies of patients with pacemakers have suggested that physiologic pacing may reduce the risk of atrial fibrillation, stroke, and death. A small, randomized study comparing physiologic pacing with ventricular pacing in patients with sinus-node disease showed higher survival, less atrial fibrillation, fewer thromboembolic complications, less heart failure, and a low-risk of atrioventricular block(6).

In addition, several retrospective studies on VVI pacing, de-

monstrating good clinical outcome with alternative to DDD pacing. In a previous study, the authors assessed the short- and long-term clinical effectiveness of dual chamber PMs compared to single chamber ventricular PMs in adults with AV block, sick sinus syndrome or both. They have showed a statistically significant trend towards dual chamber pacing being more favourable in terms of exercise capacity. No individual studies reported a significantly more favourable outcome with single chamber ventricular pacing(12). Because of their advanced age and the few symptoms they experienced, conservative treatment was chosen. This decision was certainly based on the results of the study by Toff et al(13) which showed that single chamber ventricular pacing for high-grade AV block in elderly patients does not influence the rate of death from all causes compared with dual-chamber pacing.

In previous study, Rediker and coworkers(14) investigated to identify better those subgroups of pacemaker recipients who could benefit from dual chamber pacing. 19 patients with DDD pacemakers that were physiologically paced were entered into a blinded, randomized protocol comparing long-term VVI versus DDD pacing. Exercise duration was greater during DDD compared with VVI pacing. However, it was only in the crossover subgroup that DDD pacing resulted in significant improvement in exercise performance and health perception compared with VVI pacing. These above advantages for DDD may be associated with age of patients. Because in our study, in comparison of DDD, VVI patients are older, so it may reduce survival of rate in this group.

In another study, the authors had compared two groups, one of the 1474 patients were received a ventricular pacemaker and the another of 1094 patients were received a physiologic pacemaker(15). The annual rate of stroke or death due to cardiovascular causes were higher in VVI compared with DDD pacing. The annual rate of atrial fibrillation was significantly lower among the patients in the DDD pacing, for a reduction in relative risk. The observed annual rates of death from all causes and of hospitalization for heart failure were lower among the patients with a DDD pacing than among those with a VVI pacing, but not significantly so. Physiologic pacing provides little benefit over ventricular pacing for the prevention of stroke or death due to cardiovascular causes(15). In another large randomised study, MOST (mode selection trial in sinus node

dysfunction), the short-term complication rate was substantially lower for DDD pacing.(16) Nevertheless, they assigned a total of 2010 patients with sinus-node dysfunction to dual-chamber pacing or ventricular pacing and followed them. In SND, DDD pacing does not improve stroke-free survival, as compared with ventricular pacing. However, dual-chamber pacing reduces the risk of atrial fibrillation, reduces signs and symptoms of heart failure, and slightly improves the quality of life. Overall, dual-chamber pacing offers significant improvement as compared with ventricular pacing.(17)

The decision to implant a pacemaker usually is based on symptoms of a bradyarrhythmia or tachyarrhythmia in the setting of heart disease. Symptomatic bradycardia is the most common indication. Firstly, SND is one of the main indications for pacemaker implantation. SND is a syndrome manifested by a variety of cardiac arrhythmias, including sinus bradycardia, sinoatrial block, and paroxysmal supraventricular tachycardia, which frequently alternates with periods of bradycardia or even asystole(18). There is no evidence that cardiac pacing prolongs survival in patients with sinus node dysfunction. Indeed, total survival and the risk of sudden cardiac death of patients with sick sinus syndrome are similar to that of the general population(4). A recent randomized trial reported that in SND, dual-chamber pacing does not improve stroke-free survival, as compared with ventricular pacing. However, dual-chamber pacing reduces the risk of atrial fibrillation, reduces signs and symptoms of heart failure, and slightly improves the quality of life. Overall, dual-chamber pacing offers significant improvement as compared with ventricular pacing. (19). However, the prognosis for patients who receive a pacemaker for this reason, in terms of mortality and occurrence of AF or heart failure (HF) did not really demonstrate a great superiority of dual-chamber pacemakers over single-chamber devices. However, in one of the study, the authors found that there was no significant mode-related difference in either the incidence of atrial fibrillation or any of the other prespecified clinical end points in the overall group(2). Pacemaker therapy also has no prognostic importance for bradyarrhythmia. The choice of VVI pacing influenced survival adversely, a difference which was more evident during the first two analysed decades. In a previous study, patients in the VVI groups who had had previous atrial tachyarrhythmia had a significantly higher incidence of atrial fibrillation than did those in the DDD group. Patient survival at 7 years was lower in the VVI group than in the DDD (20). In addition, DDD PMs are associated with a markedly longer survival than VVI in long-term study.(21) We also showed similar results as fourth year is higher mortality in DDD group compared with VVI group. Compared with single-chamber ventricular pacing, dual-chamber pacing can reduce adverse events and, as a result, improve quality of life in patients paced for sick sinus syndrome. For patients with sick sinus syndrome requiring pacing, dual-chamber pacing increases quality-adjusted life expectancy at a cost that is generally considered acceptable.(22)

Analysis of two prespecified subgroups — patients with SND and those with atrioventricular block at implantation — did reveal a favorable response to dual-chamber pacing in patients with sinus-node dysfunction. In a late follow-up of a prospective study of patients with SND, Andersen et al(18) reported that atrial pacing reduced embolic events, atrial fibrillation, and mortality. In patients affected by high degree AV block without preexisting congestive heart failure there is no definite

demonstration that DDD pacing gives real clinical advantages in respect to VVI pacing. Evidence suggests that physiologic pacing (dual-chamber or atrial) may be superior to single-chamber (ventricular) pacing because it is associated with lower risks of atrial fibrillation, stroke, and death. In previous study, Canadian Trial of Physiologic Pacing Investigators(23) investigated the effects of physiologic pacing versus ventricular pacing on the risk of stroke and death due to cardiovascular causes. They observed annual rates of death from all causes and of hospitalization for heart failure were lower among the patients with a physiologic pacemaker than among those with a ventricular pacemaker, but not significantly so. In the treatment of atrioventricular block, dual-chamber cardiac pacing is thought to confer a clinical benefit as compared with single-chamber ventricular pacing. DDD pacing confers potentially important hemodynamic advantages over ventricular pacing by linking the timing of atrial and ventricular contraction, a phenomenon called atrioventricular synchrony. In elderly patients with high-grade atrioventricular block, the pacing mode does not influence the rate of death from all causes during the first five years or the incidence of cardiovascular events during the first three years after implantation of a pacemaker(13).

Dual-chamber pacing is in common usage in the UK. Recipients are more likely to be younger that is similar another study because of higher life expectancy in these group. Also, it was most beneficial effect from pacing with dual-chamber devices compared with ventricular devices.(3) However, the previous study, the authors evaluated whether elderly patients who have implanted pacemakers for complete atrioventricular block gain significant benefits from DDD pacemakers compared with VVI pacemakers. They concluded that in active elderly patients with complete heart block, DDD pacing and VVI pacing yielded similar improvements in quality of life and exercise performance. However, after a short follow-up period, they noted that VVI pacing caused significant left atrial enlargement and impaired left ventricular diastolic functions(24).

The carotid sinus syndrome is a well-known cause of syncope: the cardio-inhibitory forms are the easiest to diagnose and probably the easiest to treat. A recent randomized trial failed to show any benefit of cardiac pacing in patients with carotid sinus hypersensitivity(25). We also demonstrated that none of the patients were death during fourth year outcome.

Therefore, VVI mode appears to be a good alternative to DDD pacing, considering its advantages of a single lead, in terms of procedure time shortening, risk of complication, and cost reduction. Single-chamber ventricular pacing prevents bradycardia and death from ventricular standstill, but dual-chamber pacing better emulates normal cardiac physiology by restoring atrioventricular synchrony and matching the ventricular pacing rate to the sinus rate. As a result, dual-chamber pacing, as compared with single-chamber ventricular pacing, improves hemodynamic function, but the clinical benefit is uncertain(13).

This may be related to several VVI pacing mode disadvantages. Lack of atrial stimulation contraindicates its use in patients with sick sinus syndrome. Choosing the site of atrial sensing is limited by a fixed position of the atrial detection dipole in relation to the extremity of the ventricular lead. Finally, recent study showed that age, administration of non-dihydropyridine calcium channel blockers, and AF influence the incidence of inappropriate atrial sensing. Atrial undersensing and AV dis-

sociation are known to have some clinical consequences such as exercise intolerance and rhythmological consequences. Moreover, good atrial detection seems to be correlated with quality of life.

Study limitation

The main limitation of this study is the relatively short follow-up period because of missing data collection and long term retrospective study. Because retrospective studies are flawed, pacemaker selection may not random and we also can select the more expensive forms of technology for younger, less sick patients. Assignment to DDD or VVI pacing depending on the choice of the physician, selection of specific pulse generators and leads, and individual experience and skills may have influenced the results of our study. However, full patient investigation, such as exercise stress test to exclude chronotropic insufficiency or long-term ECG Holter recording to exclude asymptomatic supra-ventricular tachycardia was not performed in all patients. This study focused on long-term clinical outcome, pacing parameters, and long-term survival. Thus, the authors can neither comment on the quality of life in the two groups. However, these questions have been the subject of former trials.

Conclusion

As a conclusion, the implantation of permanent pacemaker decreases the mortality rate. When comparing VVI and DDD pacing, the mortality rate is lower the dual-chamber pacing as compared with ventricular pacing are observed principally in the subgroup of patients with sinus-node dysfunction. Finally, because mortality rate is associated with many conditions in these groups, we cannot exactly measure the mortality rate.

Declaration of interest: No conflicts of interest.

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