Real world effectiveness of primary implantable cardioverter defibrillators implanted during hospital admissions for exacerbation of heart failure or other acute co-morbidities: cohort study of older patients with heart failure

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Cite this as: *BMJ* 2015;351:h3529
doi: 10.1136/bmj.h3529

This is a summary of a paper that was published on thebmj.com as *BMJ* 2015;351:h3529

STUDY QUESTION

What is the clinical effectiveness of primary implantable cardioverter defibrillators (ICDs) in preventing all cause mortality and sudden cardiac death in patients age ≥66 who received the device during acute admission for exacerbation of heart failure or other co-morbidities?

SUMMARY ANSWER

After adjustment for potential confounding and healthy candidate bias, in these patients primary ICD therapy was not associated with clinically or statistically significant reduction in all cause mortality or sudden cardiac death.

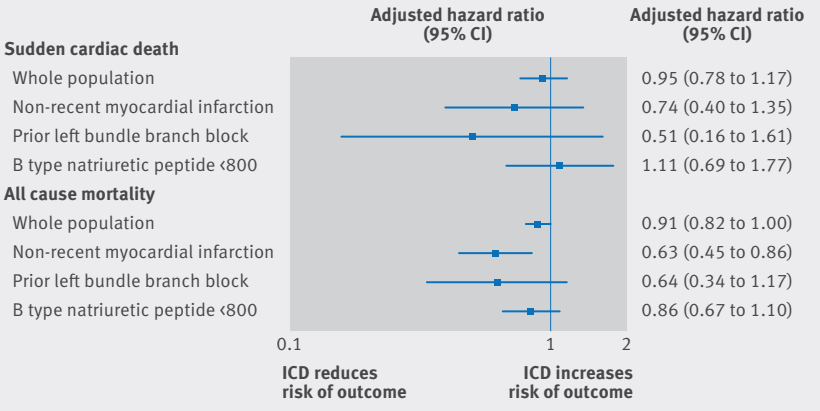
WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Trials have shown that primary ICDs can reduce mortality in younger patients with stable chronic heart failure without major co-morbidity. Subsequent observational studies confirmed findings but did not adequately control for healthy candidate bias. Moreover, the difference in survival with ICDs appeared within the first few months in the observational studies compared with after a year in the trials, suggesting contribution of other factors. The current study adjusted for mortality during the first 180 days (latency analysis) and for high dimensional propensity score. With these adjustments used to eliminate early survival differences that were probably not attributable to the ICD, the apparent difference in survival was no longer evident.

Participants and setting

Older patients (age ≥66) with acute admissions for heart failure or other co-morbidities who were eligible for primary ICD therapy in general practice settings.

Hazard ratios (adjusted for high dimensional propensity score) for death and sudden cardiac death in patients with and without ICD in latency 180 day analyses



Design, size, and duration

A retrospective cohort study with 23 111 patients (5258 with ICD and 17 853 without) admitted in 2005-08 (mean follow-up 2.8 years; maximum 5 years).

Main results and the role of chance

After adjustment for confounding and healthy candidate bias, patients who received an ICD during an acute admission for heart failure or other co-morbidity did not have a substantially different risk of sudden cardiac death (hazard ratio 0.95, 95% confidence interval 0.78 to 1.17) or mortality (0.91, 0.82 to 1.00) compared with those who had no ICD during their admission. ICD therapy was associated with a significant reduction in all cause mortality (37%) in patients with non-recent (>40 days) myocardial infarction and non-significant reductions in mortality in those with left bundle branch block (36%) or those with low levels of B type natriuretic peptide (14%).

Bias, confounding, and other reasons for caution

Our choice of a 180 day latency period was conservative and could still overestimate survival benefit. We lacked statistical power to confirm the trends seen for some subgroups. Residual confounding because of incomplete information on all mortality risk factors for heart failure, such as the New York Heart Association Class and QRS duration, probably overestimated the observed minimal benefit of ICD.

Generalisability to other populations

Our results do not apply to older patients with heart failure who undergo ICD implantation during elective admissions or as outpatients, or to those who received cardiac resynchronisation therapy with ICD. They do, however, apply to similar older patients in industrialised countries with higher burdens of heart failure and/or co-morbidities and should be considered in selection of patients or timing for primary ICD therapy.

Study funding/potential competing interests

This project was funded by the Agency for Healthcare Research and Quality (AHRQ), US Department of Health and Human Services (DHHS) as part of the Developing Evidence to Inform Decisions about Effectiveness (DEcIDE) programme, and the Centers for Medicare and Medicaid Services (CMS), US DHHS. SS and JDS have received varied funding and honorariums, full details of which are with the full version of this paper.

Avoidability of hospital deaths and association with hospital-wide mortality ratios: retrospective case record review and regression analysis

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Cite this as: *BMJ* 2015;351:h3239
doi: 10.1136/bmj.h3239

This is a summary of a paper that was published on thebmj.com as *BMJ* 2015;351:h3239

STUDY QUESTION

Is a hospital's standardised mortality ratio (SMR) associated with the proportion of deaths judged by clinicians to be avoidable?

SUMMARY ANSWER

The association was small but not statistically significant.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

This paper confirms that hospital SMRs do not provide a useful indication of the proportion of deaths that are avoidable (based on one or two medical reviewers' judgments). However, as both methods have shortcomings neither is a suitable measure for comparing the overall quality of hospitals.

Participants and setting

Deaths in acute hospital trusts in England.

Design, size, and duration

Retrospective case record review of 100 randomly selected deaths in each of 34 acute hospital trusts (deaths in 2009 for 10 trusts and in 2012/13 for 24 trusts) randomly selected from across the spectrum of one of the commonly used SMRs, the hospital standardised mortality ratio (HSMR). Avoidability of death (due to acts of omission and commission) assessed by trained medical reviewers using a six grade Likert scale (1=definitely unavoidable; 6=definitely avoidable). Avoidable deaths were those judged to have at least a 50% likelihood of having been avoidable (grade 4-6).

Main results and the role of chance

The proportion of patients in which death was judged to be avoidable was 3.6% (95% confidence interval 3.0 to 4.3). Fewer deaths were deemed avoidable in 2012/13 (3.0%, 2.4% to 3.7%) than in 2009 (5.2%, 3.8% to 6.6%), although this difference is influenced by several factors, including reviewers' greater awareness in 2012/13 of orders not to resuscitate and patients perceived to be sicker on admission. The association between HSMRs and the proportion of avoidable deaths in a hospital was small but not significant (regression coefficient 0.3, 95% confidence interval −0.2 to 0.7). A difference in HSMR of 105 and 115 would be associated with an increase of only 0.3% in the proportion of avoidable deaths. The regression coefficient was similar in both time periods (0.1 and 0.3). A similar non-significant association was observed for the other hospital-wide SMRs used in England, the summary hospital level mortality indicator: regression coefficient 0.3 (95% confidence interval −0.3 to 1.0).

Bias, confounding, and other reasons for caution

The lack of a significant association may partly reflect methodological shortcomings of both types of measure. Hospital-wide SMRs do not take into account the severity of a patient's primary condition, variation between trusts regarding clinicians' diagnostic practice, the thoroughness of recording comorbid conditions, the use of palliative or end of life coding, and availability of alternative facilities for patients, such as hospices. Retrospective case record review had only moderate inter-rater reliability (κ 0.45), and non-medical professionals were not involved. The absence of even a moderately strong association is a reflection of the small proportion of deaths (3.6%) judged likely to be avoidable and of the relatively small variation in avoidable death proportions between trusts.

Generalisability to other populations

The findings are generalisable to acute hospitals in England but need to be confirmed in other countries.

Study funding/potential competing interests

The 2009 part of this study was funded by the National Institute for Health Research research for patient benefit programme and the 2012/13 part by the Department of Health policy research programme. We have no competing interests.

Regression coefficients (95% confidence intervals) for relation* between avoidable death proportion and two commonly used hospital-wide standardised mortality ratio metrics

		Hospital standardised mortality ratio (HSMR)		Summary hospital level mortality indicator (SHMI)	
Date of case record review	No of trusts	Regression coefficient (95% CI)	P value	Regression coefficient (95% CI)	P value
Overall (2009 &2012/13)	34	0.3 (−0.2 to 0.7)	0.23	0.3 (−0.3 to 1.0)	0.29
2009	10	0.1 (−0.1 to 1.3)	0.82	−0.02 (−1.0 to 0.6)	0.56
2012/13	24	0.3 (−0.2 to 0.7)	0.26	0.5 (−0.4 to 1.3)	0.24

*Regression coefficient can be interpreted as percentage point increase in avoidable death proportion for a 10 point increase in hospital-wide SMR.

Risk of intracranial haemorrhage in antidepressant users with concurrent use of non-steroidal anti-inflammatory drugs: nationwide propensity score matched study

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Cite this as: *BMJ* 2015;351:h3517
doi: 10.1136/bmj.h3517

This is a summary of a paper that was published on thebmj.com as *BMJ* 2015;351:h3517

STUDY QUESTION

Does concurrent use of non-steroidal anti-inflammatory drugs (NSAIDs) by antidepressant users increase the risk of intracranial haemorrhage?

SUMMARY ANSWER

The combined use of antidepressants and NSAIDs was associated with an increased risk of intracranial haemorrhage within 30 days of initial combination compared with the use of antidepressants alone.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Very little is known about the risk of intracranial haemorrhage associated with the combined use of antidepressants and NSAIDs. Combined use of antidepressants and NSAIDs was associated with an increased risk of intracranial haemorrhage within 30 days of initial combination.

Participants and setting

We used Korean Health Insurance Review and Assessment Service (HIRA) claims data for patients who received a prescription for at least one antidepressant drug. The study included patients who began receiving antidepressants for the first time (index date) without a history of having received antidepressants during the preceding year. We excluded patients who had been diagnosed as having cerebrovascular diseases within a year before the index date.

Design, size, and duration

This was a retrospective nationwide propensity score matched cohort study using the HIRA database from 1 January 2009 to 31 December 2013. Among 5 835 835 new users of antidepressants, 5 168 833 met the study inclusion criteria. After propensity score estimation and matching in a one to one ratio, the cohort used in the analysis of antidepressant with versus without NSAIDs included 4 145 226 people.

Main results and the role of chance

The 30 day risk of intracranial haemorrhage was higher in patients with combined use of antidepressants and NSAIDs, compared with antidepressant use without NSAIDs (hazard ratio 1.6, 95% confidence interval 1.32 to 1.85). We found no statistically meaningful differences in risk of intracranial haemorrhage between the antidepressant drug classes and no difference in risk associated with age or intracranial haemorrhage subtype. The hazard ratio associated with concomitant use of NSAIDs was higher among male patients (hazard ratio 2.6, 1.93 to 3.42) than among females (1.2, 0.89 to 1.57). Comorbidities and comedications did not seem to increase the risk of intracranial haemorrhage with combined use of antidepressants and NSAIDs.

Bias, confounding, and other reasons for caution

This study has potential inaccuracy of coding, and the outcome measures were limited to patients admitted to hospital with intracranial haemorrhage. However, a validation study showed the overall positive predictive value of the diagnoses to be 83.4%, which indicates fairly accurate results. Also, patients with fatal events are likely to be admitted to hospital, which minimises the possibility of us missing fatal cases. We took account of selection bias and confounding with respect to the relative difference at baseline for the risk of intracranial haemorrhage between the comparison groups by using propensity score matching, which should eliminate the baseline differences.

Generalisability to other populations

The results are generalisable to patients who are taking antidepressants and NSAIDs concomitantly.

Study funding/potential competing interests

This research received no specific grant from any funding agency in the public, commercial, or not for profit sectors.

Risk of 30 day intracranial haemorrhage with combined use of antidepressants and non-steroidal anti-inflammatory drugs

Subgroup	Incidence rate per 1000 person years* (95% CI)		Adjusted hazard ratio (95% CI)	P value
	Antidepressants only	Antidepressants + NSAIDs		
Overall	1.6 (1.36 to 1.84)	5.7 (5.28 to 6.22)	1.6 (1.32 to 1.85)	<0.001
Antidepressant exposure				
TCA	1.5 (1.16 to 1.95)	5.8 (5.18 to 6.48)	1.7 (1.33 to 2.13)	0.770*
The rest	1.6 (1.35 to 1.95)	5.7 (5.02 to 6.39)	1.6 (1.27 to 2.03)	
SSRI	1.3 (0.93 to 1.79)	6.8 (5.50 to 8.48)	1.4 (1.17 to 1.72)	0.678*
The rest	1.7 (1.42 to 1.99)	5.6 (5.11 to 6.10)	1.5 (1.27 to 1.86)	
SNRI	4.3 (2.55 to 7.26)	4.4 (2.51 to 7.78)	0.4 (0.32 to 0.46)	0.190*
The rest	1.5 (1.28 to 1.75)	5.8 (5.31 to 6.27)	1.5 (1.31 to 1.83)	

SNRI=serotonin-norepinephrine reuptake inhibitors; SSRI=selective serotonin reuptake inhibitors; TCA=tricyclic antidepressants.
*P value for interaction.