Important New Evidence Service

In Partnership with The Centre for Medicines Optimisation at Keele University

ScriptSwitch™ Rapid Update 2 – April 2017

Erectile dysfunction treatment: Mortality and cardiovascular outcomes after first myocardial infarction

A recent Swedish nationwide cohort study investigated the association between treatment for erectile dysfunction (ED) and long-term outcomes in 43,145 men after their first myocardial infarction (MI). The study found that men treated for ED had reduced mortality (33%) and hospitalisation for heart failure (40%) compared with men who did not receive treatment. However, while this study is broadly reassuring about the use of ED treatments post-MI, it may be that those men who received treatment for ED were healthier than those who did not (confounding by indication).

Reference: Andersson DP, Lagerros YT, Grotta A *et al*. Association between treatment for erectile dysfunction and death or cardiovascular outcomes after myocardial infarction. Heart. Published Online First: 09 March 2017. doi:10.1136/heartjnl-2016-310746

What do we know already?

- ED is associated with an increased risk of cardiovascular disease in previously healthy men. The European Association of Urology 2017 guidelines on Male Sexual Dysfunction state that there is increasing evidence that ED can be an early manifestation of coronary artery and peripheral vascular disease, and should be regarded as a potential warning sign of cardiovascular disease.
- In a pre-specified sub-study of the ONTARGET and TRANSCEND studies (Böhm *et al*. 2010), investigators concluded that in men with cardiovascular disease, ED is a potent predictor of all-cause death and the composite of cardiovascular death, MI, stroke, and heart failure.
- There is some evidence that lifestyle modifications and drugs to reduce cardiovascular disease risk factors may help improve sexual function in men with ED (European guidelines).

What does this evidence add?

- This Swedish cohort study provides new evidence on the association between treatment for ED and mortality or cardiovascular outcomes after a first MI. The investigators found men who received treatment for ED with a phosphodiesterase-5 (PDE-5) inhibitor after their first MI had reduced mortality and lower rates of hospitalisation compared with men not receiving treatment. Alprostadil use was not associated with a reduction in mortality, although only 8.3% of men receiving ED medication were using this drug.
- The authors report that in previous studies of men with ischaemic heart disease, the prevalence of ED was around 40-50%, although only one-third of these men were receiving medicine to manage their condition. Since only 10% of men in this current study were receiving treatment for ED, the authors suggest that there was probably a large number of men in the study with ED who were not receiving medicine, meaning the reductions in mortality and heart failure hospitalisation were most likely associated with treatment for ED, not the condition itself.
- The authors of this study advised that their results should be interpreted with caution since they could not adjust for some key factors related to the use of erectile medication and prognosis, for example, marital status, smoking, physical activity, income and blood pressure. It would seem that treatment for ED is a marker of good health and of higher income, a higher likelihood of being married, higher education, and a more active and healthy lifestyle in general.

Study details

Participants:

- The study included all adult men (aged 18 to 80 years) with a first MI in Sweden. Men with previous MI, revascularisation, coronary artery bypass graft, prostatectomy or surgery for rectal cancer were excluded.

Intervention and comparison:

- Treatments for ED considered in this study were the PDE-5 inhibitors sildenafil, tadalafil and vardenafil, and alprostadil (prostaglandin E1). The majority of men who received treatment for ED received a PDE-5 inhibitor (92%).

Outcomes and results:

- The main outcomes of interest were all-cause mortality, MI and hospitalisation for heart failure, cardiovascular mortality, non-cardiovascular mortality, revascularisation and major adverse cardiac event (MACE, defined as hospitalisation for MI, or heart failure or revascularisation).
- Of the 43,145 men included in the study, 3,068 men (7%) had at least one ED medicine dispensed during a mean follow-up of 3.3 years. The men who received ED medicine had 33% lower mortality (hazard ratio [HR] 0.67, 95% CI 0.55 to 0.81) and 40% lower risk of hospitalisation for heart failure (HR 0.60, 95% CI 0.44 to 0.82) compared with those men who were not prescribed ED medication.
- The reductions appeared to be dose-dependent, with men who received 5 or more prescriptions for ED medicines having the greatest reductions. The effect was limited to PDE-5 inhibitors; men treated with alprostadil had a similar mortality to men without treatment for ED.
- Treatment for ED was also associated with a reduction in cardiovascular mortality (36%) and non-cardiovascular mortality (21%). Although the incidence rate for revascularisation was halved in men taking ED medication, after adjustment for confounders no association between treatment and revascularisation was found. The incidence rate for major adverse cardiac events (MACE) was lower in men receiving ED medication compared with no treatment (HR 0.79, 95% CI 0.68 to 0.92)
- There were some important differences between the 2 cohorts. Compared to men receiving no treatment, men treated for ED were younger (mean age 61 years *vs.* 64 years), and were less likely to have heart failure (0.6% *vs.* 2.1%), diabetes (10% *vs.* 13%), COPD (0.8% *vs.* 1.6%) or a history of stroke (3.2% *vs.* 6.0%).

Level of evidence:
Level 2 (limited quality patient-oriented evidence) according to the SORT criteria.

Study funding:
No funding source.