

Gastrointestinal disease

Bariatric surgery lowers CVD risk in severely obese patients with NAFLD

Compared with nonsurgical management, bariatric surgery is associated with a significant reduction in cardiovascular disease (CVD) risk in individuals with severe obesity and nonalcoholic fatty liver disease (NAFLD), a large, population-based retrospective cohort study from the United States has found.

To examine the association between bariatric surgery and CVD risk in individuals with severe obesity and NAFLD the authors obtained data from the MarketScan Commercial Claims and Encounters database between 2007 and 2017. The study participants were insured adults aged 18-64 years with NAFLD and severe obesity (BMI ≥ 40) but without a history of bariatric surgery or CVD before their NAFLD diagnosis.

The main outcome was the incidence of cardiovascular events in participants who had received surgical management and in those who had received nonsurgical management. The primary composite outcome included myocardial infarction (MI), heart failure, or ischaemic stroke, and the secondary composite cardiovascular outcome included secondary ischaemic heart events, such as angina pectoris, transient ischaemic attack and secondary cerebrovascular events, including acute cerebrovascular insufficiency, arterial embolism and thrombosis or atherosclerosis.

The study cohort included 86,964 adults with a mean [SD] age of 44.3 [10.9] years. More than two-thirds

were women, 59,773 (68.7%). A total of 30,300 participants (34.8%) underwent bariatric surgery while 56,664 (65.2%) received nonsurgical management. Those who received surgery had a mean 7.2 month wait between the index date and their surgery. Surgical procedures performed included 11,371 Roux-en-Y gastric bypass operations, 10,404 sleeve gastrectomies, and 8,525 other types of bariatric surgery.

Compared with those in the nonsurgical group, individuals in the surgical group were younger (43.3 vs 44.9 years; $P < 0.001$), more likely to be women (75.9% vs 64.9%; $P < 0.001$), and less likely to have a history of smoking (6.2% vs 9.4%; $P < 0.001$).

After 96 months' follow-up, 1,568 individuals in the surgical group experienced incident cardiovascular events compared with 7,215 individuals in the nonsurgical group; incidence rate difference 4.8 (95% CI: 4.5-5.0) per 100 person-years.

Bariatric surgery was associated with a 49% lower risk of CVD; adjusted hazard ratio (aHR) 0.51 (95% CI: 0.48-0.54) compared with nonsurgical management.

The risk of primary composite CVD outcomes was reduced by 47%; aHR 0.53 (95% CI: 0.48-0.59), and the risk of secondary composite CVD outcomes decreased by 50%; aHR 0.50 (95% CI: 0.46-0.53) in individuals who had undergone surgery compared with those who had not had surgery.

NAFLD has become the most common chronic liver disease in many western countries. It is the hepatic manifestation of metabolic syndrome and is strongly linked to obesity-induced insulin resistance, dyslipidaemia, and hypertension, and although there are shared risk factors, NAFLD is an important independent risk factor for CVD morbidity and mortality.

The study authors conclude: 'The findings provide evidence in support of bariatric surgery as an effective therapeutic tool to lower elevated CVD risk for select individuals with obesity and NAFLD. Although bariatric surgery is a more aggressive approach than lifestyle modifications, it may be associated with other benefits, such as improved quality of life and decreased long-term healthcare burden.'

DR JEZ THOMPSON

Elsaid MI, Bridges JFP, Brock G et al. Association of bariatric surgery with cardiovascular outcomes in adults with severe obesity and nonalcoholic fatty liver disease. *JAMA Network Open* 2022;5(10):e2235003

Respiratory disease

Azithromycin beneficial in nonsmoking COPD patients who suffer exacerbations

Long-term azithromycin confers a net benefit in COPD patients who are former smokers with a recent history of exacerbations, a model-based benefit-harm analysis has shown. The benefit is likely to be larger in those patients who suffer frequent exacerbations, the study found.

The investigators created a probabilistic model-based benefit-harm analysis of prophylactic azithromycin (250 mg/day) to prevent COPD exacerbations among patients already on maximum inhaled therapy. This simulated the course of COPD over 20 years. Benefits and harms were translated into quality of life weights to generate a single metric of net changes in quality-adjusted life years (QALYs).

The study population was derived from a large randomised controlled trial of azithromycin in COPD (the MACRO study). Patients with GOLD severity grades II to IV were considered who met exacerbation criteria.

Data from other studies were used to model expected transition from one GOLD grade to the next, background mortality was calculated from national statistics. Annual rates of exacerbations were modelled as a function of the underlying GOLD grades.

A literature scoping exercise was undertaken looking at the adverse effects of azithromycin which could potentially affect its net benefit.

The model examined the effect of the drug on the decline in GOLD stage, the prevalence of adverse events and the increase in antibiotic resistance over time. QALYs were calculated for each model state and the net QALY gain determined from the use of azithromycin. The benefit: harm ratio from different histories of exacerbations was also investigated.

In the primary target population (i.e. patients with GOLD grade $\geq$ II with at least one moderate/severe exacerbation in the past 12 months) azithromycin resulted in a net QALY gain of 17.9 per 100 patients (99.8% probability of expected QALY gain) over 20 years.

There was a higher net QALY gain in those with more frequent exacerbations (two or more moderate or at least one severe exacerbation in the previous year) of 21.8 QALYs per 100 patients (99.9% probability of expected QALY gain) over 20 years.

There was no benefit in patients who had not had a moderate or severe exacerbation in the previous year.

The authors conclude that: 'This study shows that azithromycin is very likely to be net beneficial in patients with COPD with a positive history of exacerbations.'

'Future research should evaluate the effectiveness of azithromycin in current smokers,' they add.

The NICE guideline on COPD recommends consideration of prophylactic oral azithromycin where there are troublesome exacerbations, when inhaled therapy has been optimised and the patient is a nonsmoker.¹ These findings support current NICE guidance.

DR PETER SAUL

Ahmadian S, Sin DD, Lynd L et al. Benefit-harm analysis of azithromycin for the prevention of acute exacerbations of chronic obstructive pulmonary disease. *Thorax* 2022;77:1079-87

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1 National Institute for Health and Care Excellence. NG115. Chronic obstructive pulmonary disease in over 16s: diagnosis and management. NICE. London. 2018 www.nice.org.uk/guidance/ng115

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