research

ICU stay linked to survival after STEMI p 353

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ORIGINAL RESEARCH Retrospective cohort study

Intensive care use and mortality among patients with ST elevation myocardial infarction

Valley TS, Iwashyna TJ, Cooke CR, et al

Cite this as: *BMJ* 2019;365:l1927
Find this at: http://dx.doi.org/10.1136/bmj.l1927

Study question Is admission to an intensive or coronary care unit (ICU) associated with reduced mortality among patients with ST elevation myocardial infarction (STEMI) who could have received care in either an ICU or non-ICU location?

Methods This was a retrospective cohort study of US Medicare beneficiaries admitted to hospital with STEMI between January 2014 and October 2015. Patients admitted to an ICU were compared with patients admitted to a non-ICU (general/telemetry ward or intermediate care). The primary outcome was 30 day mortality. An instrumental variable analysis was used to account for confounding, using as an instrument the additional distance that a STEMI patient would need to travel beyond the closest hospital to arrive at a hospital in the top quarter of ICU admission rates for STEMI.

Study answer and limitations Among patients who received ICU care dependent on their proximity to a hospital in the top quarter of ICU admission rates, ICU admission was associated with lower 30 day mortality than non-ICU admission (absolute decrease 6.1 (95% confidence interval −11.9 to −0.3) percentage points). The use of administrative data may limit the ability to account for certain clinical characteristics relevant to STEMI.

Association of intensive care unit (ICU) admission with 30 day mortality

Model	Absolute 30 day mortality, % (95% CI)	P value
Unadjusted results		
ICU	18.2	—
Non-ICU	13.8	—
Adjusted model		
ICU	17.0 (16.7 to 17.3)	Reference
Non-ICU	16.5 (16.1 to 16.9)	0.04
Instrumental variable model*		
ICU	14.9 (13.1 to 16.7)	Reference
Non-ICU	21.0 (17.1 to 25.0)	0.04

Models adjusted for characteristics of patients and hospitals (see tables 2 and 3 of the full paper on bmj.com). Standard errors adjusted for clustering of patients within hospitals.
*Two stage least squares regression of all patients, using differential distance to nearest hospital with high ICU admission rates as instrumental variable.

What this study adds Admission to ICU may improve mortality for patients with STEMI who could be treated in an ICU or non-ICU unit. Methods to identify patients who might benefit from ICU care are needed and should be followed by randomised trials to test the effect of expanded access to ICU and the mechanisms that result in benefit from ICU.

Funding, competing interests, and data sharing This work was supported by the National Institutes of Health (K23HL140165, K12HL138039, R01HL137816). Medicare data are not publicly available but can be obtained through the Center for Medicare and Medicaid Services. The statistical code for analyses is included online, and additional code can be obtained from the corresponding author.

Surgical interventions for stress urinary incontinence

ORIGINAL RESEARCH Systematic review and network meta-analysis of randomised controlled trials

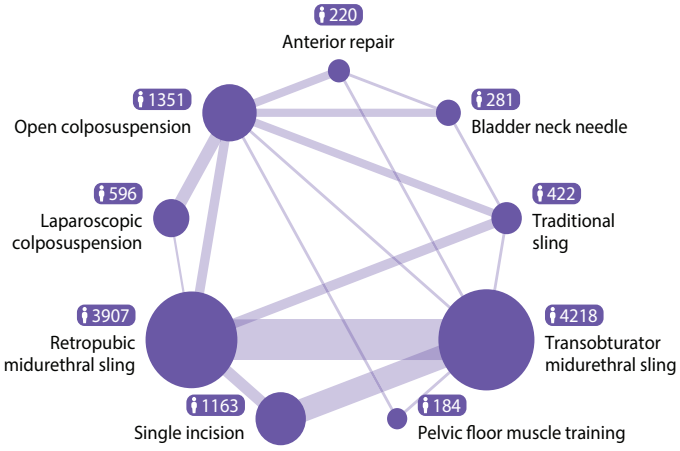
Surgical interventions for women with stress urinary incontinence

Imamura M, Hudson J, Wallace SA, et al

Cite this as: *BMJ* 2019;365:l1842
Find this at: http://dx.doi.org/10.1136/bmj.l1842

Study question How do the different surgical treatments for women with stress urinary incontinence compare with each other for effectiveness and safety?

Methods The authors used statistical methods to combine data from multiple randomised controlled trials on nine surgical treatments for stress urinary incontinence. Cochrane reviews and the Cochrane Incontinence Specialised Register were searched for relevant randomised controlled trials up to May 2017. Trials were eligible for inclusion if they compared surgery with another surgery for the treatment of stress urinary incontinence in women. The effectiveness of surgery was assessed in terms of cure (resolution) or improvement of incontinence symptoms, as well as adverse events and complications after surgery.



Network plot for number of women showing cure of stress urinary incontinence symptoms. Circle size reflects number of women and line width reflects number of direct comparisons

COMMENTARY Women and surgeons must navigate a challenging landscape of choices

Stress urinary incontinence—defined as leaking urine with coughing, sneezing, or exertion—affects more than one in 10 women,[1] and represents a large unmet health need. The linked systematic review and network meta-analysis by Imamura and colleagues provides a unified summary of comparative efficacy and safety for all contemporary surgical procedures for stress urinary incontinence.[2]

Pelvic mesh

From the late 1990s, there has been a rapid progression in surgical techniques for management of stress incontinence. The advent of the polypropylene midurethral sling seemed to many surgeons like a revolutionary advance, compared with earlier and more invasive options such as open colposuspension and native tissue fascial slings. The midurethral sling was a technically simple day-case procedure, with excellent efficacy rates and seemingly lower morbidity than previous procedures. It rapidly became the most widely offered procedure in many countries,[3] and with its popularity, overall surgical treatment rates increased.[4]

However, increasing publicity about the harms of pelvic mesh, including chronic pain and vaginal erosions, have caused a crisis of confidence among both the public and surgeons.[3] Implantation of midurethral slings has declined, even in countries where they are not currently restricted or suspended,[5 6] and with this decline, overall treatment rates for stress incontinence appear to have fallen.[7 8]

Existing trials are of short duration, and underpowered for serious but rarer adverse events such as mesh complications

This systematic review comes at a crucial time in the debate about pelvic mesh, as clinicians have struggled to integrate older evidence about colposuspension and native tissue fascial slings with newer evidence from more than 150 randomised trials published as retropubic, transobturator, and single incision polypropylene sling devices came to market. The work reported here has already been used to inform the recent National Institute of Health and Care Excellence (NICE) guidelines[9] on surgical management of stress urinary incontinence, which despite controversy,[10] are likely to shape future practice in England and beyond.

The interpretation of results from such a complex network meta-analysis is itself complex,[11] and the results have to be considered in the light of a wider range of evidence, including observational studies. Imamura and colleagues identify retropubic slings, transobturator slings, traditional fascial slings, and open colposuspension as the procedures likely to be the most effective.

This focus obscures important differences in efficacy and safety between these procedures. Both the direct and indirect comparisons reported here favour retropubic slings over transobturator slings, with moderate confidence in this difference. NICE have therefore recommended specifically against the use of transobturator slings, except where a retropubic approach would be contraindicated.

Another concern is in the assessment of the evidence for laparoscopic colposuspension. No statistically significant difference exists in the cure or improvement rates between open and laparoscopic colposuspension; therefore, for many women, laparoscopic colposuspension might remain preferable in view of reduced morbidity.

Bulking agents

As the mesh controversy has developed, women have more often chosen urethral bulking agents as first line surgical treatment. Although the efficacy of bulking agents is moderate at best, the safety profile is good.[12] Here, because no randomised trials were available to bring bulking agents into the network meta-analyses, they could not be included in the evidence synthesis,

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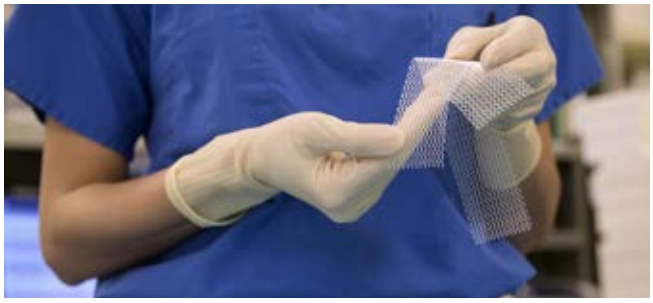


Study answer and limitations 175 trials with a total of 21 598 participants met the inclusion criteria. Most were of moderate to low quality. Studies that followed women for up to one year were pooled and showed that interventions with highest cure rates were traditional sling, retropubic midurethral sling (MUS), open colposuspension, and transobturator MUS (rankings of 89.4%, 89.1%, 76.7%, and 64.1%, respectively). For improvement of incontinence symptoms, the same four interventions were most likely to be the most effective (rankings of 67.7%, 97%, 63.8% and 76.1%, respectively). Evidence was limited for adverse events. For the comparison between retropubic MUS and transobturator MUS, repeat surgery and groin pain were more likely after transobturator MUS, and suprapubic pain, vascular complications, bladder or urethral perforation, and voiding difficulties were more likely after retropubic MUS. Evidence was limited for long term postoperative complications. Most trials had weaknesses in the way they were conducted and reported, making the conclusions of the current study less robust.

What this study adds Retropubic MUS, transobturator MUS, traditional sling, and open colposuspension are more effective than other procedures for stress urinary incontinence in the short to medium term. Data on long term effectiveness and adverse events are, however, limited.

Funding, competing interests, and data sharing This work was funded by the National Institute for Health Research Health Technology Assessment Programme (project No 15/09/06).

See the full paper on bmj.com for competing interests. No additional data available.

Study registration PROSPERO CRD42016049339

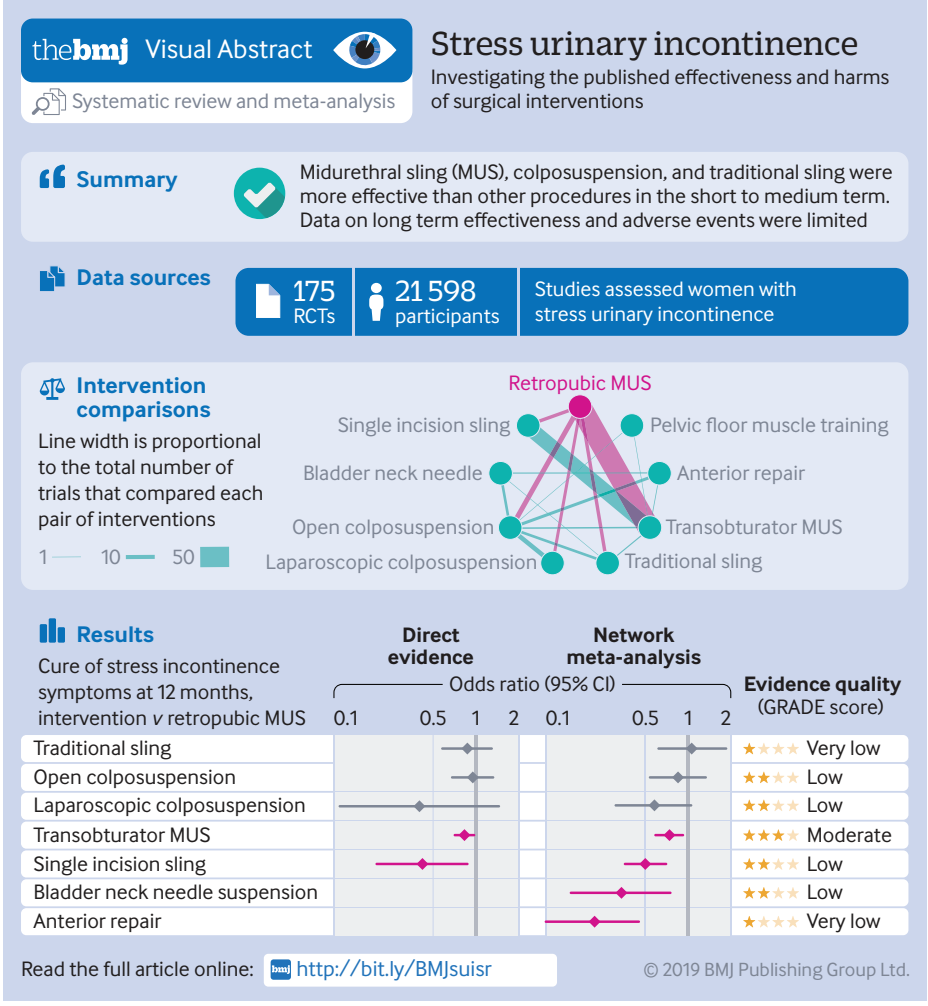
but remain a reasonable low risk option to discuss with patients.

While NICE have developed a decision aid[13] to help women choose between so many surgical options, further work is clearly needed to understand how women should navigate what remains a complex choice, based on their individual priorities.[14] Imamura and colleagues' work highlights the huge difficulties in establishing adequate evidence of comparative long term safety. The existing randomised controlled trials are of short duration, and even in aggregate are underpowered for serious but rarer adverse events such as mesh complications, which can occur many years after implantation.[15]

These safety issues could be even more pronounced if women will increasingly opt for colposuspension and traditional slings, which are both highly technical and operator dependent, but which have been neglected for almost two decades. This shift in practice will create huge challenges in the training or retraining of current and future gynaecologists and urologists. There remains a real risk that regulators, surgeons, and the public will reject the midurethral sling in favour of procedures that are eventually proven to have been both less safe and less effective.

Cite this as: *BMJ* 2019;365:l2350

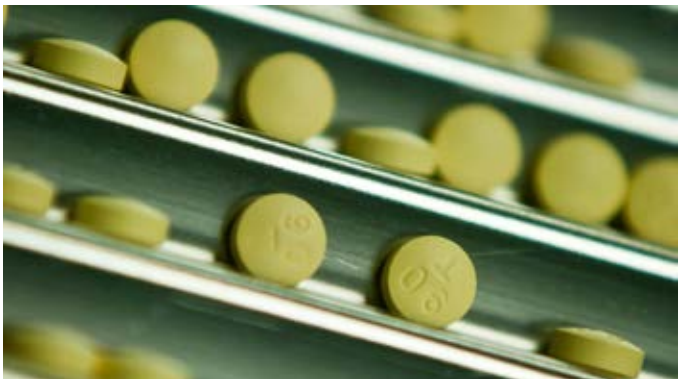
Find the full version with references at http://dx.doi.org/10.1136/bmj.l2350



Ticagrelor plus aspirin versus clopidogrel plus aspirin for platelet reactivity in patients with minor stroke or transient ischaemic attack

Wang Y, Chen W, Lin Y, et al; on behalf of the PRINCE Protocol Steering Group

Cite this as: *BMJ* 2019;365:l2211
Find this at: http://dx.doi.org/10.1136/bmj.l2211



Study question How does the safety and efficacy of a ticagrelor+aspirin combination compare with a clopidogrel+aspirin combination when used to reduce high platelet reactivity and stroke recurrence at 90 days in patients with minor stroke or transient ischaemic attack?

Methods This trial was conducted at 26 centres in China (August 2015 to March 2017). Safety and clinical outcomes of ticagrelor (180 mg loading dose, 90 mg twice daily thereafter) were compared with those of clopidogrel (300 mg loading dose, 75 mg daily thereafter) on a background of aspirin (100 mg daily for the first 21 days) in 675 patients with acute minor stroke or transient ischaemic attack over 90 days. The primary outcome was the proportion of patients with high platelet reactivity (measured as P2Y12 reaction units ›208). High platelet reactivity is the resistance or non-responsiveness to antiplatelet agents and is a known marker for recurrent ischaemic events. Secondary outcomes included high platelet reactivity at 90 days in patients carrying genetic variants that would affect clopidogrel metabolism (that is, the CYP2C19 loss-of-function alleles), and any stroke (ischaemic or haemorrhagic) recurrence at 90 days, six months, and one year.

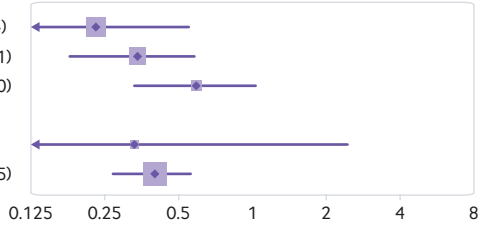
Study answer and limitations At 90 days, high platelet reactivity occurred in 35 (12.5%) of 280 patients in the ticagrelor+aspirin group and 86 (29.7%) of 290 patients in the clopidogrel+aspirin group (risk ratio 0.40, 95% confidence interval 0.28 to 0.56; P<0.001); high platelet reactivity occurred in 10.8% versus 35.4% (0.31, 0.18 to 0.49; P<0.001) of patients carrying CYP2C19 loss-of-function alleles. The rate of major or minor haemorrhagic events did not differ between the ticagrelor+aspirin and clopidogrel+aspirin groups (4.8% *v* 3.5%; P=0.42). Stroke occurred in 21 (6.3%) of 336 patients in the ticagrelor+aspirin group and 30 (8.8%) of 339 patients in the clopidogrel+aspirin group (hazard ratio 0.70, 95% confidence interval 0.40 to 1.22; P=0.20). As this is a phase II trial, these results would need to be replicated and investigated further in larger studies and in different populations. Safety outcomes at one year follow-up should also be looked at in future studies.

What this study adds This study suggests the efficacy of ticagrelor+aspirin in reducing high platelet reactivity in patients with minor stroke and transient ischaemic attack, especially in carriers of the CYP2C19 loss-of-function alleles at 90 days after the onset of symptoms.

Funding, competing interests, and data sharing Details on funding and competing interests are in the full paper on bmj.com. The technical appendix, dataset, and statistical code are available from the corresponding author.

Study registration ClinicalTrials.gov NCT02506140.

Outcome Phenotype	Ticagrelor+aspirin No with event/total No (%)	Clopidogrel+aspirin No with event/total No (%)	Hazard ratio or risk ratio (95% CI)	Hazard ratio or risk ratio (95% CI)	P value	P for interaction
HOPR at 90 days						
Poor	4/38 (10.5)	14/33 (42.4)		0.23 (0.07 to 0.55)	0.004	
Intermediate	12/113 (10.6)	41/124 (33.1)		0.34 (0.18 to 0.58)	<0.001	
Extensive	16/117 (13.7)	25/119 (21.0)		0.59 (0.33 to 1.03)	0.07	0.42
Ultra	0/1 (0.0)	2/5 (40.0)		NA		
Unknown	1/6 (16.7)	2/4 (50.0)		0.33 (0.02 to 2.44)	0.29	
Total	33/275 (12.0)	84/285 (29.5)		0.40 (0.27 to 0.56)	<0.001	



HOPR (high on-treatment platelet reactivity)=P2Y12 reaction units of more than 208, as measured by the VerifyNow P2Y12 assay; NA=not applicable.
Effect of ticagrelor+aspirin versus clopidogrel+aspirin on high platelet reactivity in trial participants at 90 days, stratified by metaboliser status. Patients with two *2 or *3 alleles were classified as having a poor metaboliser phenotype, those with one *2 or *3 allele were classified as having an intermediate metaboliser phenotype, those without a *2, *3, or *17 allele were classified as having an extensive metaboliser phenotype, and those with one *17 allele and *17 homozygotes were classified as having an ultra-metaboliser phenotype. A total of 321 patients in the ticagrelor+aspirin group and 329 patients in the clopidogrel+aspirin group were included in the genetic analysis.