

considered. Firstly, the value of a change to outpatient practice should only be investigated in the context of an existing optimised fast-track programme, that is it should not be a justification for units without an existing properly implemented fast-track programme. Secondly, it may be more difficult to implement in some settings, such as hospital vs ambulatory surgery centres (ASC). However, preliminary data suggest an outpatient programme can be performed successfully in both settings.<sup>11</sup>

In addition to these contextual factors, the most important challenge for future improvement within the outpatient ERAS setting is better understanding and control of undesirable perioperative pathophysiological responses such as pain relief, control of inflammatory responses and orthostatic intolerance, optimal blood management, and prevention of cognitive dysfunction.<sup>12</sup> Future optimisation and reduction of these post-surgical sequelae therefore represent a prerequisite for further development and increased use of outpatient total hip arthroplasty and total knee arthroplasty. There is a need to be able to identify patients at risk of complication or re-admission preoperatively and before discharge. Of special importance will be the need to identify ways to predict high pain and inflammatory responders<sup>12</sup> so that related pathophysiology can be modified to facilitate optimal post-discharge rehabilitation strategies.<sup>2</sup>

Nevertheless, for high-performing total hip arthroplasty and total knee arthroplasty ERAS centres, outpatient surgery is a natural evolution, and the results have led to widespread enthusiasm for the approach across healthcare systems, industry, and media. However, for some patients it may remain better to prolong their hospital stay modestly. This may apply especially to sites without an already established successful fast-track protocol, where outpatient arthroplasty may not be possible or lead to increased re-admissions and morbidities. In addition, the outpatient approach should not be based upon increased use of post-discharge care facilities with secondary cost and safety challenges.

To summarise, there is a delicate balance between implementation of established evidence for total hip arthroplasty and total knee arthroplasty ERAS care and moving too fast to more widespread implementation of the promising outpatient approach given the fact that more patients with comorbidities or need for revision surgery are being seen. We should be mindful to 'walk before we run' and remember that the ERAS concept is based on reduction of undesirable pathophysiological responses to surgery in order to enhance recovery, meaning 'first better, then faster'.

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## Could anaesthetic technique be blocking successful outcomes in arteriovenous fistula surgery?

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### Declarations of interest

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Over 25,000 people in the UK and 500,000 people in the USA are currently on haemodialysis, with the number increasing by 2.5% year-on-year.<sup>1,2</sup> Kidney disease has a significant impact on both longevity and quality of life, with survival from end-stage renal disease (ESRD) worse than most cancers.<sup>3</sup> ESRD also places considerable demand on healthcare resources. Frequent hospitalisation of patients on haemodialysis, coupled with the cost of renal replacement therapy, means that 3% of the UK National Health Service budget is expended on kidney failure services.<sup>4</sup> In the USA this figure totalled \$35.9 billion and accounted for 7.2% of Medicare paid claims in 2019.<sup>2</sup>

Vascular access is the key modifiable risk factor that determines both patient experience and outcome on haemodialysis.<sup>5</sup> Hospitalisation, which has a negative impact on health-related quality of life,<sup>6</sup> is three times less likely in patients dialysing via an arteriovenous fistula (AVF) compared to a central venous catheter (CVC).<sup>5</sup> AVFs also deliver better quality dialysis with fewer infective and thrombotic complications, and ultimately patient survival is improved compared to using CVCs or arteriovenous grafts (AVG).<sup>5,7</sup> Despite these benefits the most recent UK Renal Registry Multisite Dialysis Access Audit highlighted that nearly 80% of dialysis units in England, Wales and Northern Ireland still fall short of established targets for numbers of patients dialysing via an AVF or AVG.<sup>1,8</sup> A major obstacle to meeting such criteria is the failure of many newly created AVFs to mature, with failure rates approaching 50%.<sup>9</sup>

### Determinants of fistula maturation

Creating a well-functioning AVF often means 'placing an unphysiological high flow construct into an ill vascular bed'.<sup>10</sup> Once surgically fashioned, fistula maturation is a dynamic process whereby vascular remodelling occurs to permit enlargement of the outflow vein. Blood flow through the artery increases and the vein wall subsequently thickens to allow cannulation. The arterial supply and venous outflow are critical to success, as is surgical technique,<sup>10,11</sup> but why maturation fails thereafter remains incompletely understood.<sup>12</sup>

Flow through the fistula at 24 h has been found to correlate with patency at 12 weeks.<sup>13</sup> Poor flow, as one component of Virchow's triad, predisposes to thrombosis, and thrombosis is the commonest reason for AVF failure within 72 h of surgery.<sup>14</sup> Beyond this time failure appears to be related to development of stenoses secondary either to pre-existing vessel trauma, or to intimal hyperplasia and vessel remodelling that occurs as a result of increased shear stress following creation of the arteriovenous anastomosis.<sup>15</sup> Pharmacological strategies including aspirin, clopidogrel, fish oils and glyceryl trinitrate patches, and non pharmacological strategies such as exercise and infrared therapy have all been studied but most do not confer any significant clinical benefit.<sup>16</sup>

### Can anaesthetic technique influence fistula success rate?

Regional anaesthesia (RA), local anaesthetic (LA) infiltration and general anaesthesia (GA) all represent potential anaesthetic options for AVF surgery. Unlike LA infiltration, RA blocks not only motor and sensory nerves but also sympathetic nerves, resulting in vasodilatation, reduced vaso-spasm and increased blood flow through the new AVF.<sup>17,18</sup> Whilst GA also results in intra-operative vasodilatation, such potentially beneficial vasodilatation will not persist beyond emergence to the extent associated with RA. Furthermore, the comorbidities associated with, and resulting from, ESRD increase the risk of perioperative complications secondary to GA in this group of patients.<sup>19</sup> Based on the associated intra- and post-operative haemodynamic changes, RA for AVF surgery therefore represents a theoretically plausible intervention that might reduce early thrombosis and subsequent AVF failure.

### Local versus regional anaesthesia

Most AVF in the UK are currently created under either LA or RA.<sup>20</sup> Several non-randomised<sup>21,22</sup> and subsequent small randomised studies suggested better early patency rates for AVF created under RA.<sup>23–25</sup> Our (AJRM, EA) single-centre randomised controlled trial (n=126) remains the largest to date and showed better early to medium term (3 months) patency rates for AVF created under a single-shot brachial plexus block compared to LA (84% vs 62%; odds ratio [OR] 3.3 [95% CI 1.4 to 7.6] p=0.005).<sup>18</sup> The AVF failure rate in the LA group of 38% was comparable to rates observed in other randomised trials of pharmacological interventions to prevent AVF failure.<sup>9,26</sup> In long-term follow up we observed a higher rate of 1 yr functional patency using RA compared to LA (68% vs. 49%; OR 2.1 [95% CI 1.5 to 2.7, p=0.008], with the greatest differences noted in radiocephalic AVF.<sup>27</sup> Our concurrent health economic analysis, which is limited to the UK context, also established that despite anaesthetic staff and equipment costs RA resulted in net cost savings of £195.10 per patient at 1 yr due to the reduction in new AVF procedures and CVC-related complications. An incremental cost-effectiveness ratio of ~ £12,900 per quality-adjusted life year was calculated over a 5 yr time horizon.

Importantly, this study from our group represents practice in a single centre. Similarly, three of the four studies, including ours, examined in a 2017 meta-analysis (n=286) that showed significantly lower failure rates with RA vs LA were single-centre studies. Methodological limitations leading to a risk of bias were also present in some of the trials, therefore leading to calls for a large definitive trial with longer follow up.<sup>28</sup>

## General versus regional anaesthesia

In the US, the majority of AVF are created under GA, alone or in combination with LA or RA.<sup>29</sup> Whilst two retrospective studies have found better AVF outcomes and lower rates of re-operation and healthcare utilization with RA, a third retrospective analysis found GA to be associated with lower rates of early AVF failure.<sup>29–31</sup> Such conflicting findings, along with the potential for residual confounding in retrospective analyses, highlights the need for future randomised studies comparing RA to GA for AVF surgery.

## Current guidance and practice

European Society for Vascular Surgery (ESVS) guidelines recommend *considering*, and European Renal Association-European Dialysis and Transplant Association (ERA-EDTA) guidelines suggest, *but do not recommend*, RA for all primary AVF.<sup>16,32</sup> The ERA-EDTA guidance states that changing practice from LA to RA may lead to ‘unwanted complications, increased costs and delays’. The Kidney Disease Outcomes Quality Initiative guidance, developed in the USA, states that the choice of anaesthesia technique should be based on institutional experience, operative technique and patient characteristics.<sup>11</sup>

There remains significant variation in the choice of anaesthesia for AVF creation around the UK. In a recent survey, RA was used for < 10% of AVF in a third of units, with reasons cited as ‘surgeon preference, too time consuming, no regular anaesthetist available, lack of facilities or lack of robust evidence’.<sup>19</sup> Ultimately there remains a need for definitive evidence in order to change practice and policy, with key questions remaining to be answered including: Can our original findings be replicated across multiple centres by clinicians with differing degrees of expertise in and familiarity with RA for AVF surgery? Does RA actually deliver sustained, clinically-relevant differences in functional patency or simply alter early AVF flow dynamics? Are patient-centred outcomes improved with RA vs LA? Do the potential benefits of RA translate into reproducible healthcare cost savings?

## The future

Progress is occurring in improving the evidence base available to inform decisions between LA and RA for AVF surgery. The National Institute for Health Research recently commissioned a large multicentre trial comparing LA and RA for primary radiocephalic and brachiocephalic fistulae. Funding has been awarded to the ‘Anaesthesia Choice for Creation of arteriovenous fistulae’ (ACCESS) study (Health Technology Assessment NIHR 130567). The trial, led by our team in Glasgow, is due to commence recruitment in Spring 2021, and aims to randomise 566 patients from 12–20 centres across the UK over 2 yr. The primary outcome will be 1 yr unassisted functional patency, recognising the importance of functionality and ability to cannulate as a patient-related outcome measure. Important safety endpoints, quality of life scoring systems and a health economic evaluation will inform commissioners and policy makers, whilst the large sample size will facilitate modelling and sensitivity analysis for variables such as AVF site and the availability of a block room. More generally, this work may help serve as a model for comparisons of RA to GA for AVF surgery, as well as randomised trials in other surgical contexts within and beyond vascular surgery that rigorously

compare regional blocks to other techniques across multiple institutions, focusing on patient-centred and functional outcomes.

We hope the results of the ACCESS trial will be available by early 2025. In the meantime, the anaesthetic choice for AVF surgery outwith centres recruiting to the trial must be based on the best available evidence and recommendations above, taking into account as always risks and benefits in each individual, patient choice and the experience and availability of anaesthetic practitioners. There is still much to be understood about what blocks maturation of the arteriovenous fistula. Although early results are promising, it remains to be seen whether RA truly improves long-term patient and surgical outcomes in a cost-effective manner.

## Authors’ contributions

All authors contributed to the drafting, revision and final approval of the manuscript.

## Declarations of interest

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## Monitoring of nociception: is more always more?

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