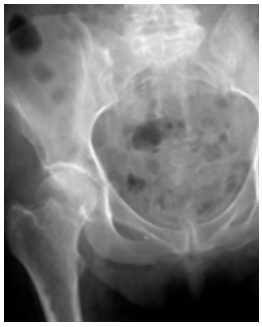
Treatment of displaced intracapsular hip fractures in older patients

Total hip arthroplasty is preferable to hemiarthroplasty in healthy patients



MEDICAL-ON-LINE/ALAMY

RESEARCH, p 1397

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In the linked systematic review, Hopley and colleagues compare outcomes after total hip replacement versus hemiarthroplasty when treating displaced femoral neck fractures in older patients.[1] Hip fractures cause considerable death and disability in elderly people. Worldwide, 1.6 million new hip fractures occurred in 2000, and these accounted for the loss of 2.35 million disability adjusted life years (DALYs) annually and 1.4% of the burden of disease in women in the Western world.[2] The incidence of hip fractures is estimated to rise to more than six million in 2050, around half of which will be femoral neck fractures.[3]

Displaced femoral neck fractures in elderly people are treated by internal fixation or prosthetic replacement, with either a hemiarthroplasty replacing the femoral head and neck or a total hip arthroplasty which also includes acetabular replacement. These treatments are associated with different complication rates, function, and independency of living. Hemiarthroplasty produces consistently better function than internal fixation,[4-6] and lower reoperation rates (10% *v* 40%).[7] No significant differences have been seen for mortality, perhaps because individual studies and reviews lack sufficient statistical power to detect them.[8] Internal fixation is therefore mainly used for undisplaced fractures, whereas arthroplasties are favoured for displaced fractures. Hemiarthroplasty has been more popular than total hip arthroplasty, perhaps because total hip arthroplasty had inferior results in some early reports.[9] However, over the past few years, an increasing body of evidence supports the use of total hip arthroplasty instead of hemiarthroplasty in a selected group of physically and mentally fit patients.[10]

In Hopley and colleagues' systematic review and meta-analysis, data from 15 studies, seven of which were randomised, and 1890 arthroplasty procedures showed a lower risk of reoperation after total hip arthroplasty compared with hemiarthroplasty (relative risk 0.57, 95% confidence interval 0.34 to 0.96, risk difference 4.4%).[1] Furthermore, total hip arthroplasty showed better hip function after one to four years (mean difference 5.4/100 points in Harris hip score). No significant difference was seen for the risk of dislocation (1.48, 0.89 to 2.46) and other general complications (1.14, 0.87 to 1.48).

Ten of the 15 studies included only physically and mentally fit patients, and the rest did not specify patient related inclusion criteria. Thus, the results may not be representative of the average patient with a femoral neck fracture. In addition, only seven of the 15 studies were randomised, and proper concealment of randomisation was reported in only four. Even if a selection bias in the non-randomised studies could not be shown, the observational and randomised studies differed. The lower risk for reoperation after total hip arthroplasty was mainly driven by the observational studies, the benefit disappeared when the high quality studies were analysed separately. The same tendency was seen for dislocations, whereas hip function was consistently better after total hip arthroplasty.

A wide variety of prosthetic implants were used in the studies. In the total hip arthroplasty group important details like femoral head size and surgical approach may have affected the dislocation rates. Hemiarthroplasties were unipolar or bipolar and uncemented or cemented. When modern hemiarthroplasties are used, cemented and uncemented stems seem to perform equally well.[11] Bipolar designs, with dual articulation between the large femoral head and the acetabular cartilage and between the head and femoral stem, were introduced to improve hip movement and function, but their benefits have yet to be proved.[12]

Although many different hemiarthroplasties have been used with good results, it is generally accepted that old monobloc cementless types, like the Austin Moore prosthesis, should be avoided because early loosening and subsidence lead to impaired function.[7] The use of this prosthesis may have skewed the functional results in favour of total hip arthroplasty.

Nevertheless, the review shows that total hip arthroplasty is a safe procedure in fit patients with femoral neck fracture, and that it produces better functional results than hemiarthroplasty. However, total hip arthroplasty may be associated with a higher rate of complications and a reoperation rate of 0-9% is still reported in the included studies. Thus, there is room for future improvement for both hemiarthroplasty and total hip arthroplasty. Prosthetic design, with use of larger heads or (semi-) constrained joints, and the choice of surgical approach, may reduce dislocation rates and other complications. Along with patient selection, these factors should be included in further studies. Long term results are also needed; total hip arthroplasty may result in mechanical complications such as dislocations and acetabular loosening, which level out early functional benefits.

While awaiting such evidence, both forms of hip replacement should be considered complementary treatment modalities. Surgeons should tailor treatment individually and in particular evaluate comorbidities, ambulatory status, and cognitive function. Physically and mentally fit patients may have better functional results with total hip arthroplasty than with hemiarthroplasty. Frailer patient should still be treated with a modern type hemiarthroplasty.

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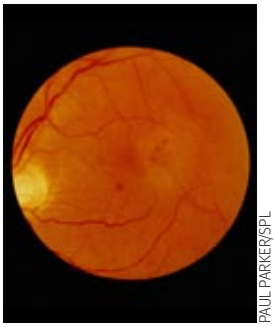
Bevacizumab for the treatment of neovascular age related macular degeneration

Controversy remains about the off label use of bevacizumab



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RESEARCH, p 1398

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The era of biological agents for the management of neovascular age related macular degeneration was firmly ushered in when two randomised controlled clinical trials in 2007 found that ranibizumab, a monoclonal antibody to vascular endothelial growth factor, improved visual outcomes in patients with this condition.[1 2] However even before the original trial data were released, ophthalmologists had already begun to treat patients with neovascular age related macular degeneration with bevacizumab (the parent molecule of ranibizumab), which is licensed for intravenous administration in advanced colorectal cancer. In the linked study, Tufail and colleagues report their findings from the ABC Trial, a multicentre randomised controlled study that compared the use of bevacizumab and ranibizumab for the treatment of neovascular (wet) age related macular degeneration.[3]

Originally ophthalmologists administered bevacizumab intravenously but soon changed to intraocular delivery because of the potential for systemic adverse events.[4 5] Intraocular delivery vastly reduced the dose of bevacizumab, which meant that the commercially available preparation (for intravenous use in the treatment of cancer) could be dispensed into hundreds of 1.25 mg aliquots. Users calculated the dose on the basis of the intravitreal dose of ranibizumab used in the trials. Several non-randomised studies of intraocular bevacizumab subsequently reported improvement or stabilisation of vision in neovascular age related macular degeneration on a par with that seen after treatment with ranibizumab.[6] These reports have led to the widespread use of bevacizumab in preference to ranibizumab, mainly because it is substantially cheaper.

Although bevacizumab was acceptable as a treatment for neovascular age related macular degeneration when there were no effective alternatives, once ranibizumab received approval for use in the condition, debate began about whether it should be used in preference to bevacizumab. The effects of these drugs on visual outcomes have not been compared in trials of adequate size. Furthermore, the safety of bevacizumab for ocular administration has not been as rigorously tested as has that of ranibizumab in controlled clinical trials.[1 2] Several recent systematic reviews concluded that the widespread off label intravitreal administration of bevacizumab was not justified in the absence of objective evaluations of bevacizumab relative to representative controls and of head to head trials with ranibizumab.[6 7] Many large trials comparing the two drugs are under way on several continents.

Tufail and colleagues assessed the efficacy of bevacizumab compared with a control group. Controls received no treatment, photodynamic therapy, or intravitreal pegaptanib sodium administered at six weekly intervals, which was the usual standard of care that was available in the NHS at the time that the trial was enrolling participants.[3] Bevacizumab was given as a loading phase of three treatments followed by six weekly review intervals with defined criteria for retreatment. The retreatment algorithm used was more similar to usual clinical practice than the mandatory monthly treatments used in the original ranibizumab clinical trials.[1 2] Significantly more people taking bevacizumab had improved visual acuity by more than three lines compared with controls at one year (32.3% v 3.0%; adjusted odds ratio 18.1, 95% confidence interval 3.6 to 91.2; number needed to treat 4, 3 to 6). Reassuringly, mean best corrected visual acuity was not reduced in people treated with bevacizumab during follow-up.

Although the ABC Trial fills a gap in the evidence base and showed robustly that bevacizumab is better than no treatment, photodynamic therapy, or six weekly intravitreal pegaptanib sodium, it does not tell us whether the drug is as effective as ranibizumab. Several studies and a recent small single centre randomised controlled study that published its six month findings found no differences in efficacy between ranibizumab and bevacizumab in the short term.[8-11]

The ABC Trial provides valuable data on systemic and ocular adverse events. Even though participants were too

few to allow safety signals to be detected reliably, the trial found no differences in the frequency of ocular adverse events between the two arms on the basis of standardised grading of the fundus. These findings help to alleviate concerns raised recently by several small retrospective studies, which suggested that bevacizumab might be associated with a higher risk of subretinal bleeding.[1 2]

The potential for systemic adverse events is still a concern in patients who receive intraocular therapy that is aimed at inhibiting vascular endothelial growth factor. Although the likelihood of systemic exposure is low, circulating antibodies were detected in the peripheral blood of participants in the ranibizumab trials. This strongly suggests that the drug can leak from the eye in sufficient amounts to elicit a systemic immunological response and raises the possibility that patients are at increased risk of arterial thromboembolic events.[1 2] No published data exist to suggest that bevacizumab enters the systemic circulation after intraocular administration, but similar mechanisms may exist, and absence of serious adverse arterial thromboembolic events in the bevacizumab arm of the ABC Trial is therefore reassuring. Nonetheless, the off label use of bevacizumab should not be encouraged until the large randomised trials comparing it with ranibizumab report their findings.

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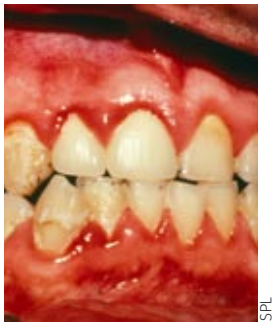
Periodontal disease and poor health outcomes

Clinicians must recognise the risks and refer patients for periodontal care



SPL

RESEARCH, p 1400

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Periodontal diseases are localised gingival infections that affect most adults at some time in their lives. They are broadly divided into two groups. Gingivitis is related to dental plaque and manifests as superficial redness, swelling, and bleeding of the gums. Periodontitis occurs when the infection spreads into the deeper tissues surrounding the roots of the teeth, and it causes breakdown of the gingival tissues and alveolar bone resorption.

Evidence shows that periodontal diseases can have systemic effects.[1-3] Oral infection can result in the formation of sites that favour colonisation by blood borne microbes—a locus minoris resistentiae. A well known example of this phenomenon is heart valves that are damaged by rheumatic fever, which are more susceptible to bacterial infection from blood borne bacteria.

In the linked survey, de Oliveira and colleagues report that poor oral hygiene (measured by self reported toothbrushing) is associated with a higher risk of cardiovascular disease (hazard ratio 1.7, 95% confidence interval 1.3 to 2.3) and low grade inflammation (C reactive protein and fibrinogen).[1] A prospective cohort study of 9760 people who participated in the National Health and Nutrition Examination Surveys (NHANES I and III) found that people with active periodontitis had a significantly higher risk of coronary heart disease (adjusted relative risk 1.25, 96% confidence interval 1.06 to 1.48).[4] In men under 50 years at baseline, the risk of dying from coronary heart disease was even higher (1.72, 1.10 to 2.68).[4] Periodontitis and poor oral hygiene were associated with total mortality more than with coronary heart disease itself. Similar results were reported in the Health Professionals Follow-up Study,[2 5] and in a recent meta-analysis of observational studies.[6] Other studies report that cardiovascular disease is the most commonly found systemic condition in people with periodontitis.[3]

The nature and direction of the association is unclear because periodontitis and cardiovascular disease share similar risk factors. However, it is now accepted that periodontitis has effects beyond the oral cavity, and its treatment and prevention may contribute to the prevention of vascular diseases such as atherosclerosis.[7]

Periodontal diseases are also associated with other systemic diseases including rheumatoid arthritis,[7-9] glomerulonephritis, inflammatory bowel disease,[8] diabetes, and obesity.[3 7 8] Septic pulmonary emboli involving *Streptococcus intermedius* and *Actinobacillus actinomycetemcomitans* from periodontal lesions have been found in infective endocarditis and brain abscesses.[2]

Mothers with a history of preterm delivery and low birthweight babies have worse periodontal disease than mothers with normal sized, full term babies, even after adjustment for

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Listen to coauthor Richard Watt talk about the study's findings at www.bmj.com/podcasts

confounding factors such as age, smoking, drug use, nutrition, and systemic disease.[2 10 11] It seems that a combination of high levels of periodontal pathogens and a low maternal IgG antibody response to periodontal bacteria during pregnancy is associated with an increased risk of preterm delivery.[11 12]

What are the practical implications for clinicians? A key shared risk factor in cardiovascular disease and periodontal disease is smoking. Smokers are six to seven times more likely to have alveolar bone loss and three to five times more likely to have severe periodontal disease than non-smokers.[2 3] Consequently, doctors should explain the risks of smoking for both diseases and encourage and support their patients to stop.

Young adults with premature and multiple loss of teeth and patients with systemic diseases who are resistant to medical treatment warrant particular attention. They should be referred for periodontal assessment and treatment to eliminate oral foci of infection that may be adversely affecting treatment.

In addition, it has been suggested that eliminating active infection from the oral cavity before surgical procedures, especially prosthetic surgery, may help prevent postoperative infection.

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Should oxygen be given in myocardial infarction?

On the basis of physiological reasons and no trial evidence of harm: yes

CHAGNON/SPL

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A systematic review published this week found no evidence that giving inhaled oxygen to people with acute myocardial infarction improves pain and survival, and that it may even do harm.[1] Undoubtedly the medical community will take note of such a conclusion, but are the results reliable and what do they mean for clinical practice?[2]

The review identified three randomised controlled trials that compared giving air with giving oxygen in people with an acute myocardial infarction; 387 people were studied and 14 died. The pooled relative risk of death was 2.88 (95% confidence interval 0.88 to 9.39), and this risk was 3.03 (0.93 to 9.83) in an intention-to treat analysis. Pain was also not significantly different between the groups (pooled relative risk 0.97, 0.78 to 1.20).[3-5]

Clinical classification of different types of myocardial infarction

- Type 1—Spontaneous myocardial infarction related to ischaemia caused by a primary coronary event, such as plaque fissuring or rupture
- Type 2—Myocardial infarction secondary to ischaemia resulting from an imbalance between oxygen demand and supply, such as coronary spasm
- Type 3—Sudden death from cardiac disease with symptoms of myocardial ischaemia, accompanied by new ST elevation or left bundle branch block, or verified coronary thrombus by angiography. In this type of myocardial infarction death occurs before blood samples can be obtained
- Type 4—Myocardial infarction associated with primary percutaneous coronary intervention
- Type 5—Myocardial infarction associated with coronary artery bypass graft

Methodology was poor in all three of the analysed articles, however. Two studies were performed unblinded,[2 3] one was reported in a foreign language with only an abstract accessible in English,[3] and one randomised double blind study—the largest of the three trials—was published 34 years ago at a time when reperfusion treatment for infarction did not exist.[4]

The most important outcome in trials of myocardial infarction is mortality, for which none of the three trials found a significant difference. The largest study reported nine deaths in the oxygen group and three in the pure air group.[4] In another trial, which focused on pain relief, only one death occurred, and ironically it was not even reported in the publication, and when asked later the authors did not remember in which arm of the study the death had occurred.[2] The final study reported one death in the oxygen group.[3] In the meta-analysis of these studies the result remained non-significant.[1] In conclusion, these studies provide no evidence that oxygen increases mortality.

Other aspects are worth considering. Oxygen therapy in stable angina pectoris is a cornerstone of treatment because this disease is caused by a lack of oxygen supply

to the ischaemic myocardium. Its role in this context is undisputed. Importantly, evidence shows that overt or silent ischaemia is detected after myocardial infarction in high proportion of patients, even in the era of reperfusion treatments. For example, the Swiss Interventional Study on Silent Ischemia Type II (SWISSI-II), performed before stents were used, assessed 1057 patients after myocardial infarction and found imaging evidence of silent ischaemia in 411 patients (39%).[5] Similarly, the Danish Multicenter Randomized Study of Invasive versus Conservative Treatment in Patients with inducible Ischemia after Thrombolysis in Acute Myocardial Infarction (DANAMI) investigated an ischaemia driven reperfusion strategy in more than 1000 patients after thrombolysis and estimated that more than 8% of the entire population of patients presenting with infarction would later have residual ischaemia.[6]

Another aspect to consider is the evidence on the use of hyperbaric oxygen in myocardial infarction. These studies were correctly excluded in the recent meta-analysis because they looked at a different system of giving oxygen. Nevertheless, a systematic review published in 2005 concluded that hyperbaric oxygen may improve pain relief and reduce major complications in myocardial infarction.[7] If inhaled oxygen truly was harmful an equally adverse effect from hyperbaric oxygen would be expected, yet the opposite seems to be true.

Finally, the topic of reperfusion injury in the course of acute myocardial infarction is still not settled. Initial mechanistic theories have built on the oxygen free radical pathway.[8] Oxidative stress is thought to occur on successful reperfusion, conferring an additional necrotic stimulus that leads to worse outcomes after infarction. Unfortunately, many studies in animals and patients that have tried to circumvent this phenomenon by scavenging oxygen free radicals have been ineffective. This speaks indirectly against a harmful effect of oxygen.

What does this all mean for practising clinicians? To date, no contemporary high quality study has investigated inhaled oxygen as part of the treatment of myocardial infarction, and this should be remedied. Because this systematic review found no significant difference in mortality between people taking pure air or oxygen it is reasonable to continue giving oxygen to people with acute myocardial infarction. Pathophysiological reasoning together with trial evidence of residual ischaemia after infarction support this approach.

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GMC guidance on end of life care

Important changes for clinicians take effect on 1 July

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The recently published guidance from the General Medical Council (GMC) on end of life care comes into force on 1 July 2010 and commands the attention of all doctors in the United Kingdom by emphasising that failure to comply will place registration at risk.[1]

Change became essential following the Mental Capacity Act 2005 and after reviews reported how patients with terminal illness are denied informed choice regarding the remainder of their life and the manner in which they die.[2] Doctors have been seeking advice from the GMC on these difficulties and should reasonably expect the regulatory body to provide unequivocal guidance on optimal care and how professional censure can be avoided. This last aspect became particularly important after legal challenge to the previous guidelines, in which it was held that medical opinion would not determine a patient's best interests.[3]

The GMC's standards and ethics reference group responded by initiating a review in 2007 under an outside chair, with a consultation involving all potential interest groups, and validated by independent audit.

The key conceptual changes to clinical practice are that death should become an explicit discussion point when patients are likely to die within 12 months, and that medical paternalism on the subject, however benignly intended, must be replaced by patient choice (box). Doctors will be expected to document that they have considered end of life care, discussed it with the patient or their representative, liaised and communicated within any multidisciplinary team, and recorded the results in an unambiguous and accessible way. Simultaneous compliance with current standards of informed consent is expected,[4] with the patient able to review their decision at any time.

New nomenclature includes the replacement of "artificial" with "clinically assisted" in relation to nutrition and hydration, to accommodate both medical and lay opinion that these represent basic aspects of care. The concept of "best interests" has also been supplanted by "overall benefit," which seems to deviate from the terminology of relevant case law and statute, but potentially offers a

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KEY POINTS WITHIN THE GMC END OF LIFE GUIDANCE

Fundamental principles
- A presumption in favour of prolonging life
- Compliance with the law

New terminology
- "Overall benefit"
- "Clinically assisted" nutrition and hydration

Mandated expectations
- Identification of patients approaching the end of life
- Provision of information on this matter
- Determination of preferences regarding life sustaining treatment including cardiopulmonary resuscitation
- Documentation of the above in an unambiguous and accessible format
- Communication of decisions within relevant healthcare teams

Additional guidance
- Endorsement of the Mental Capacity Act 2005
- Validating an advance refusal
- Role of the next of kin
- Withholding information
- Dealing with uncertainty and resolving disagreement
- Patients with disability
- Considering organ donation
- Care after death
- Neonates and young children

more impartial and enduring interpretation than a short-term evaluation of "medical best interests." However, the principles for reaching a decision on both these aspects remain unchanged.

The guidance will probably trigger professional debate rather than be considered definitive in all areas, and four examples for discussion are given here. Firstly, the guidance inevitably emphasises decision making in cardiopulmonary resuscitation, given the public dissatisfaction that triggered previous government policy.[5] However, it may be timely to move away from a preoccupation with cardiopulmonary resuscitation, which occurs at the end of life, and concentrate on earlier life sustaining treatment about which the patient should definitely be granted an opinion, because this is likely to influence both the incidence of cardiac arrest and the outcome from resuscitation.

Secondly, closer scrutiny is needed on how disagreements are resolved and apparent GMC endorsement of the courts "as a constructive way of thoroughly exploring the issues."[1] Specific cases show that this is not only time consuming and expensive for all parties, but may further polarise entrenched positions,[6] leading media commentators to question the merits of this course of action.[7] Empathy, communication, compromise, and mediation are fundamental to prevention and resolution of differences of opinion, and a court application should be viewed as a failure of process until proved otherwise.

Thirdly, the GMC has been notably concise about defensible administration of analgesia and sedatives at the end of life, despite the backdrop of extensive public, professional, political, and legal debate on "assisted suicide."[8] Although the ultimate point of reference has to be the law, a doctor has a duty to relieve suffering as well as pain,[9] and the responsibility to tailor a good death, as defined by the patient, is the central principle of this guidance. Instructions from other professional bodies "to avoid actions that might be interpreted as assisting, facilitating or encouraging a suicide attempt," [10] may compromise effective symptom control for fear that this may be arbitrarily construed as criminal, and it would have been helpful to resolve these concerns.

Fourthly, it is unclear whether the guidance applies only when patients are likely to die within the next 12 months, and therefore only to specialties managing progressive incurable disease and only when the clinician is confident about the prognosis. Logically, the principles should apply whenever there is a substantial (as defined by the patient) risk of death, and they should equally apply therefore to surgical specialties proposing operations on elderly people with high levels of comorbidity. This would require liaison with critical care colleagues for advice on the reversibility of complications and the implications of intensive care and subsequent health status, before determining the patient's choice of life sustaining treatment. However, many patients would find it difficult to establish an absolute position on all possible scenarios, and they might prefer to rely on medical practitioners exercising "benign paternalism" and accommodating the views of next of kin if complications arise. This mirrors the public response in other jurisdictions where advance directives have been placed on a statutory footing.[11] The benefits for most patients and practitioners of a flexible and responsive approach to care should not unwittingly be lost on a rigid platform of self determination, a concern that is relevant to the interpretation of advance directives.[12]

It is unrealistic however to expect the guidance to incorporate all current or future nuances, and it is anticipated that the medical specialties, ethical bodies, and indeed the GMC will consider the directives and offer additional advice where needed on specific scenarios. If used constructively, the guidance is an important opportunity for the profession to re-establish public confidence after the shortcomings that made this guidance necessary.

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