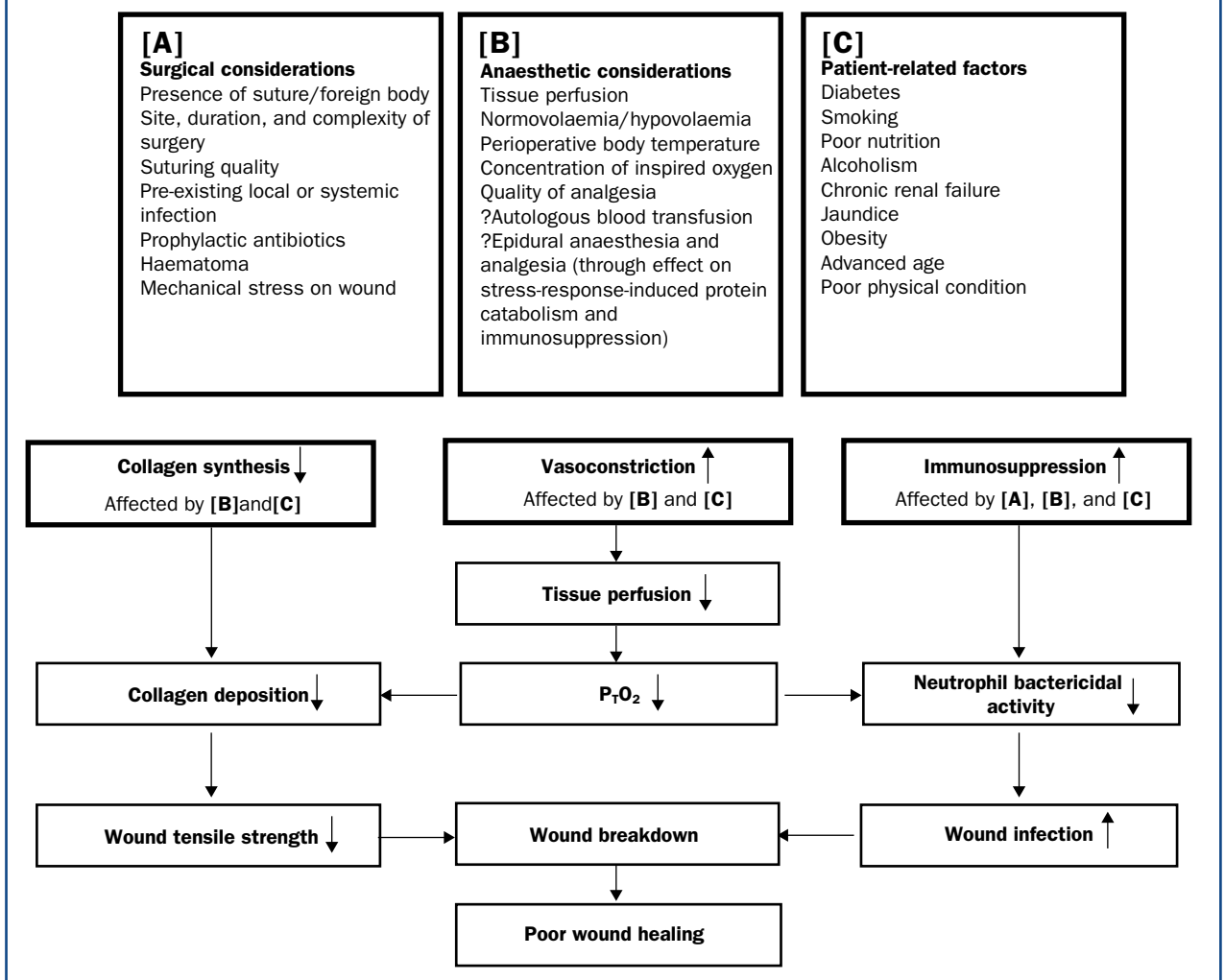
Can anaesthetic management influence surgical-wound healing?

Delay or failure of healing of surgical wounds, usually a result of infection, is arguably the commonest cause of postoperative morbidity, long hospital stays, and increased costs. 9–27% of patients undergoing colorectal surgery acquire a wound infection, which delays discharge by 5–20 days and substantially increases medical costs.[1] Although examination of the factors contributing to surgical-wound infection and healing has generally focused on surgical issues, there are also patient-related factors. In addition, new evidence is emerging that many features of perioperative care within the remit of the anaesthetist are influential in promoting wound healing (figure).

Successful surgical wound healing requires resistance to wound infection, which depends on adequate tissue perfusion to convey oxygen, neutrophils, nutrients for cellular re-growth, and systemically administered antibiotics.[2] Tissue oxygen partial pressure (P_TO_2) is especially important, because it influences both the bactericidal ability of neutrophils and the amount of scar formation, which reflects wound tensile strength.[3,4] The degree to which molecular oxygen is converted by neutrophil oxygenase to bactericidal superoxide radicals is proportional to P_TO_2.[3] So is collagen deposition, though only up to a point, because hydroxylation of proline and lysine required to form cross-links between collagen strands is catalysed by oxygen-dependent hydroxylases, and the Michaelis-Menten constant of proline hydroxylase for oxygen is about 25 mm Hg. Thus collagen deposition is independent of absolute P_TO_2 values above this level.[4]

The factors controlling tissue perfusion are encapsulated by the Hagen-Pouseille Law, according to which perfusion is directly related to tissue perfusion pressure (ie, the difference between mean arterial pressure and local tissue pressure) and inversely related to tissue vascular resistance and blood viscosity.[5] The anaesthetist's job is to maintain haemodynamic stability perioperatively, by balancing anaesthetic depth and analgesia against surgical stimulation and fluid loss. Hypovolaemia must be corrected to prevent autonomically mediated compensatory vasoconstriction, which would impair tissue perfusion.[6] Concern has been expressed that correction of profound anaemia by allogeneic blood transfusion might have an immunosuppressant effect, which could predispose to surgical-wound infections. However, two randomised, controlled trials comparing

Factors affecting surgical-wound healing



P_TO_2 = Partial pressure of oxygen in tissues

allogeneic with autologous blood transfusion yielded conflicting results in terms of overall postoperative infection rates, so whether allogeneic blood transfusion predisposes to surgical-wound infection requires further study.[7,8]

Inadvertent core hypothermia (<2°C below normal core body temperature) occurs almost invariably during surgery and is due to anaesthetic-induced thermoregulatory impairment, which results in redistribution of body heat from core to periphery.[9] Immunity against surgical-wound infection is impaired in hypothermic patients, directly because mild hypothermia inhibits neutrophil function,[10] and indirectly by postoperative thermoregulatory vasoconstriction, which decreases P_TO_2.[9] Therefore, the hypothesis that prevention of inadvertent intraoperative hypothermia would reduce the incidence of surgical-wound infection was tested. Patients undergoing colorectal surgery were randomised to either a standard-care group, who received no special active warming measures during surgery, or a normothermia group, who received active intraoperative thermal warming designed to maintain their core temperature at above 36·5°C (with a forced-air warming device and warmed intravenous fluids).[11] Intraoperative core temperature reached 34·7°C (SD 0·6) in the hypothermia group, compared with 36·6°C (0·5) in the normothermia group (p<0·001). Surgical-wound infections (defined as culture-positive pus on any postoperative day until discharge or 2 weeks later in clinic) developed in 19% of the hypothermia group, compared with 6% of the normothermia group, (p=0·009), with time to suture removal and discharge from hospital prolonged in the hypothermia group (by 1·0 and 2·6 days, respectively).[11] Therefore, anaesthetists' attention to preventing inadvertent core hypothermia during surgery is likely to reduce the incidence of surgical-wound infection by two-thirds and shorten hospital stay by about a fifth.

Surgery and postoperative pain evoke profound neuroendocrine and cytokine activity known as the "stress response". Consequent activation of the sympathetic nervous system may also cause arteriolar vasoconstriction, which reduces P_TO_2. 30 patients undergoing knee surgery were randomly assigned to receive intra-articular local anaesthetic or placebo at the end of surgery, with postoperative pain being managed with patient-controlled opioid analgesia. Pain scores were significantly higher and P_TO_2 values significantly lower (86[SD15] *vs* 111[33] mm Hg) in the placebo group, which shows that poor postoperative analgesia reduces P_TO_2 and suggests that optimisation of postoperative analgesia would also reduce surgical-wound infections.[12] Confirmation of this finding in a randomised, controlled clinical trial is warranted.

Another logical anaesthetic intervention is to increase the concentration of oxygen given intraoperatively and postoperatively. The critical period for developing surgical-wound infection is during surgery and the first 2–3 postoperative hours. 500 patients undergoing colorectal surgery were randomly assigned standard 30% inspired oxygen or 80% inspired oxygen intraoperatively and for 2 h postoperatively. Only 5% of patients receiving the higher concentration of oxygen had a surgical-wound infection, compared with 11% among those receiving standard oxygen therapy.[13] However, collagen deposition was similar in the two groups, which suggests that healing in the absence of wound infection is not improved by supplemental oxygen. Reassuringly, subgroup analysis among patients receiving high concentrations of inspired oxygen demonstrated no adverse pulmonary effects such as atelectasis and, surprisingly, the occurrence of postoperative nausea and vomiting was halved.[14,15]

Each of the three randomised controlled trials by the Outcomes Research Group cited above[11–13] were well controlled for confounding variables, including age, smoking, physical and nutritional status of the patient, presence of malignancy, volume and type of intraoperative fluid or blood, duration of surgery, and use of prophylactic antibiotics. However, it is possible that elements of anaesthetic practice other than maintenance of normothermia, optimisation of analgesia, and provision of supplemental oxygen may have a role in surgical-wound healing. Most general anaesthetics cause transient immunosuppression and many mediators of the surgical stress response are direct immunosuppressants.[16] Epidural anaesthesia and postoperative epidural analgesia preserves immune function, probably by attenuating the stress response, and is associated with a reduction in rate of postoperative pulmonary infections.[17] Used in combination with general anaesthesia, epidural anaesthesia and analgesia also reduces postoperative loss of body protein, by attenuating decrease in muscle synthesis, which is associated with the surgical stress response.[18] Because collagen formation is central to scar formation, it seems reasonable to hypothesise that combined general-epidural anaesthesia, with postoperative epidural analgesia, might preserve collagen synthesis and improve surgical-wound healing. Whether epidural anaesthesia and analgesia specifically reduces the incidence of surgical-wound infection by either of these mechanisms remains to be elucidated in a randomised controlled trial.

Improving surgical-wound healing thus requires an appreciation of patient-related risk factors and anaesthetic considerations as well as surgical technique. Partnership between surgeons, anaesthetists, and nurses should ensure that all reversible risk factors and preventive strategies are fully exploited to avoid the common and costly complication of failure of wound healing.

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Will laser replace TURP for the treatment of benign prostatic hyperplasia?

Technical innovations that replace open surgery are meant to lessen the impact of such procedures on patients while maintaining efficacy. In urology, the introduction of extracorporeal shockwave lithotripsy (ESWL) to treat urinary calculi converted a major operation into a procedure that could be carried out in less than an hour with very little postoperative morbidity. Randomised clinical trials (RCT) of ESWL were difficult to carry out since having an incision was thought to be a considerable drawback to patients. However, one mistake made early in the use of ESWL was to assume that it was the best way to treat all stones. It is now clear after many years of experience that ESWL, percutaneous nephrolithotomy, and open surgery each have a place in the treatment of urinary calculi.

Similar lessons may well apply to another urological procedure. One of the most important innovations in urological surgery was the introduction of transurethral resection of the prostate (TURP) about 70 years ago. Since then, the surgical techniques for TURP have improved, the equipment has been modernised, and indications for treatment have been standardised. Most urologists would now agree that TURP is the "gold standard" for patients with benign prostatic hyperplasia (BPH) who need surgical treatment. It has taken many years for TURP to achieve this status, and the reason for this delay in acceptance may well have been the dearth of RCTs comparing TURP with open surgery.

In 1989, two reports had a substantial impact on urologists' views of TURP. Mebust and colleagues[1] showed that among 3885 patients undergoing TURP, the mortality rate was 0·2% and the postoperative-complication rate 18%. Although the mortality rate was not deemed excessive, there was concern about the postoperative morbidity: the factors that contributed to complications were long resection time, large size of the prostate gland, and pre-existing medical disorders. The second report, a retrospective study of about 53 000 men from three countries, found that long-term age-specific mortality rates were higher for TURP than open prostatectomy, and that more patients in the TURP group required a second operation.[2] Further studies have shown that the excess mortality was unlikely to have been caused by the operation itself; instead it was more likely to have been related to co-morbidity.[3] In addition, the National Prostatectomy Audit confirmed the efficacy of TURP.[4]

The effect of these studies was an increase in research into the cause, epidemiology, and treatment of BPH. It also stimulated the search for a therapy that was less traumatic and less invasive than TURP. A greater understanding of the cause of lower-urinary-tract symptoms led to the discovery of drugs that were investigated in large multicentre RCTs. Because of these RCTs the urologist knows exactly how effective drug treatment is and, most particularly, the exact place it occupies in the management of BPH.

At the same time that drugs were being studied, several technological innovations were made, all aimed at reducing complications while maintaining the efficacy of TURP. Various types of heat treatment, such as microwave therapy, needle ablation, and laser treatment, were evaluated in open studies (some inordinately large) or RCTs (most of which were too small or of too short a duration) from which information about long-term outcomes could not be drawn. Yet many urologists carry out laser treatment for BPH. One of the early RCTs of laser and TURP found that, although the efficacy was similar, the number of complications after laser therapy was greater, particularly those of prolonged catheterisation, bacteriuria, and urethral irritation.[5]

Further developments in laser technology have led to the use of the holmium laser, a pulsed solid-state laser that was originally used to break up urinary calculi. The device has a side-firing fibre that was at first used to vaporise, but now enucleates, the prostatic adenoma.[6] Although short-term results with this technique are excellent, and the morbidity low (less than 18%), adequately powered long-term studies are lacking, which makes it difficult to assess laser therapy as a replacement for TURP. There have been several studies with 1-year follow up, and the improvement in symptom score and peak urinary flow are similar to results from TURP (panel). A longer follow-up of an RCT comparing TURP with endoscopic laser ablation of the prostate (ELAP) was recently reported by W J McAllister and colleagues.[7] The efficacy and complications had been similar at 1 year in the 151 patients randomly assigned TURP or ELAP.[8] Follow-up at 5 years showed a higher frequency of revision surgery in those originally treated by ELAP (38%) than in those treated by TURP (16%). The researchers conclude that ELAP should not be used routinely in the management of BPH.

Outcomes of RCT for BPH at 1 year

		Symptom score*	Peak urinary flow rate (mL/s)
Cowles et al[5]	Laser	10·0	5·3
	TURP	15·7	7·0
Gilling et al[6]	Laser	17·7	16·3
	TURP	18·7	11·3
Anson et al[8]	Laser	10·4	5·8
	TURP	13·1	11·8
Narayan et al[9]	Laser	16·9	9·9
	TURP	17·1	13·5
Keoghane et al[10]	Laser	12·2	4·3
	TURP	13·6	9·8

*Low scores=fewer symptoms