Introduction

Nowadays, the laparoscopic approach has become the operation of choice for a variety of procedures, including the treatment for symptomatic gallstones, gastroesophageal reflux and benign colonic diseases. Moreover, reports have shown that laparoscopic colon surgery is technically feasible and capable of fulfilling oncological criteria for cancer surgery [1–5]. However, due to the rapid introduction and ethical constraints that preclude randomization, most laparoscopic techniques become standard treatment without the backup of comparative scientific data.

In general, laparoscopic techniques are thought to provide enormous benefits to patients including: faster recovery, shorter hospital stay, reduced postoperative morbidity, prompt return to normal activities and superior cosmetic results. However, not all of these suggested clinical advantages of the laparoscopic approach can be demonstrated after blind randomization. A recently published study, comparing cholecystectomy using either laparoscopy or mini-laparotomy, showed no clear differences between the groups for hospital stay, time back to work and time to full activity [6].

One of the most important putative advantages of laparoscopic surgery is thought to be the reduction of the extent of surgical trauma [7]. Postoperative changes in the systemic immune response are proportional to the degree of surgical trauma and subsequent immune suppression may be implicated in the development of infectious complications and tumor metastasis formation. Laparoscopic surgery reduces the magnitude of the operative trauma and is thought to preserve postoperative immunological defenses.

Abstract

Background: Immune suppression is an established consequence of surgical stress and trauma. Postoperative changes in the systemic immune system are proportional to the degree of surgical trauma and subsequent immune suppression may be implicated in the development of infectious complications and tumor metastasis formation. Laparoscopic surgery reduces the magnitude of the operative trauma and is thought to preserve postoperative immunological defenses.

Methods: Relevant literature concerning postoperative immune functions and laparoscopic surgery was reviewed and clinical implications are discussed.

Results: The influence of laparoscopic surgery on the postoperative systemic immune response is significantly less after laparoscopic cholecystectomy than with the conventional approach.

Few immunological data are available concerning more advanced laparoscopic procedures. Various animal model studies of postoperative septic complications and tumor growth show that the postoperative preservation of the systemic immune response after laparoscopic surgery can have enormous clinical advantages.

Conclusion: Laparoscopic surgery preserves the postoperative immunological defenses. In the future, this may imply a lower number of infections, less local recurrence and even fewer distant metastases. Prospective randomized studies are necessary to see whether these suspected advantages can be demonstrated in clinical practice.

Key words Laparoscopic surgery · Systemic immune response
tions and tumor metastasis formation [8–10]. In the present review, an overview is given of the available literature, including our own data (unpublished data, a randomized trial, laparoscopic versus conventional Nissen fundoplication), concerning laparoscopic surgery and postoperative immune function.

Systemic immune response

The immunological response to surgery has been increasingly studied since the introduction of minimally invasive techniques. Laparoscopic surgery reduces the magnitude of the operative trauma. If alterations in the systemic immune response are proportional to the extent of injury, then the response to the laparoscopic technique will be reduced when compared with conventional surgery. Comparative studies between the two techniques of a certain type of surgery will offer the biological foundation of what is frequently described as the advantages of laparoscopic surgery. In recent years, a number of studies have been performed concerning the systemic immune response to laparoscopic surgery, both in animal models and in clinical settings.

Cytokines and the acute-phase response

Cytokines and the acute-phase response (APR) are necessary for the immune function of the host, but overproduction or production at non-inflammatory sites may, in certain cases, lead to deleterious effects on the surrounding tissue [11, 12]. A reduced production of cytokines and, thereby, a reduction of the inflammatory response is therefore thought to be beneficial for the patient’s postoperative course.

Many of the non-hepatic manifestations of the APR, such as fever, leukocytosis and tachycardia, have been attributed to tumor necrosis factor-α (TNF-α) and interleukin-1 (IL-1) [13], whereas changes in hepatic protein synthesis are mainly caused by IL-6 [14]. TNF-α and IL-1 are important cytokines in the activation of the systemic immune response and play a central role in initiating the cascade of inflammatory mediators and the subsequent activation of leukocytes that make up the immune response. Elevated plasma levels are usually not demonstrated after conventional or laparoscopic surgery; however, significantly higher levels of IL-1, during and 6 h after conventional cholecystectomy when compared with the laparoscopic approach, have been described [15].

Both IL-1 and TNF-α mediate their actions through receptors on the surface membrane which, apparently in response to the same stimuli that are known to induce their production, are shed into the circulation (IL-1ra and sTNFr-P55 and P75). These soluble receptors are thought to antagonize and regulate the activity of both cytokines [16]. Unpublished data from our laboratory show that both types of sTNF receptor can be demonstrated after laparoscopic and conventional surgery, but no significant difference between the two procedures were observed. IL-1ra has also been demonstrated after both laparoscopic and conventional surgery. In contrast to the sTNF levels, plasma levels of IL-1ra were significantly lower after the laparoscopic approach, indicating less inflammation [17].

IL-6 is a multifunctional cytokine that is involved in the modulation of host defense mechanisms, such as local inflammation, and coordinates the systemic reaction known as the APR [14]. Plasma IL-6 levels are known to be proportional to the magnitude of the surgical operation and a predictor of postoperative complications [18]. Roumen et al. describe significant differences in postoperative IL-6 levels after laparoscopic cholecystectomy [19], an observation which has frequently been confirmed by others [15, 17, 20–28]. However, the results concerning other surgical procedures show conflicting data. Hill et al. reported that the response of inflammatory mediators to hernia repair is not modified by undertaking the procedure laparoscopically. Perhaps the magnitude of the surgical injury from an open hernia repair is not large enough to demonstrate any significant reduction in the cytokine response after a minimally invasive laparoscopic repair [29]. However, reports on more advanced laparoscopic procedures are also inconclusive. Harmon et al. described a significant blunting of the IL-6 response with the use of laparoscopic techniques for colectomy compared with standard laparotomy [30], but these data were not confirmed by others. Postoperative IL-6 levels have even been found to be higher after a laparoscopic approach. Johnson et al. studied IL-6 levels after conventional and laparoscopic assisted colectomy in dogs and found significantly higher IL-6 levels after the laparoscopic approach [31]. Stage et al. confirmed these results in a clinical study comparing laparoscopic with open colonic resection for adenocarcinoma [32].

A possible explanation for the observed differences in postoperative IL-6 responses after colonic resection may be found in the techniques that were used (laparoscopic assisted or the more invasive facilitated approach) or in the diversity of the patients included. Also, both benign and malignant diseases were studied. More studies are necessary to elucidate whether the observed advantages of a reduced inflammatory response, seen after laparoscopic cholecystectomy, also hold in case other laparoscopic procedures.

The most frequently studied acute-phase protein after laparoscopic surgical trauma is C-reactive protein (CRP). Postoperative CRP levels have been found to be significantly lower after the laparoscopic approach the first 2 days after surgery [15, 19, 20, 23, 26–28, 33, 34]. Measurement of other acute-phase proteins does not show the same results. van der Velpen et al. measured post-