



Review

The impact of the type and severity of postoperative complications on long-term outcomes following surgery for colorectal cancer: A systematic review and meta-analysis



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ABSTRACT

Background: This systematic review investigated the impact of complications by type (infective vs. non-infective) and severity (using the Clavien Dindo scale) on long-term outcome following surgery for colorectal cancer.

Methods: A systematic review was performed using appropriate keywords. Meta-analysis using a random effects model was performed.

Results: 14 studies were included with a total 18,611 patients. Infective complications had a significant impact on disease free (HR 1.41, 95%CI 1.08–1.83, $p=0.01$) and overall survival (1.37 95%CI 1.22–1.55, $p<0.001$). Non-infective complications had no significant impact on either disease free (HR 1.21, 95%CI 0.97–1.52, $p=0.09$) or overall survival (HR 1.35, 95%CI 0.92–1.97, $p=0.12$). Complication severity had a significant impact on both disease free (HR 1.41, 95%CI 1.18–1.68, $p<0.001$) and overall survival (HR 1.45, 95%CI 1.25–1.69, $p<0.001$).

Discussion: Both type and severity of postoperative complications have an impact on long-term survival following surgery for colorectal cancer.

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1. Introduction

Surgical resection continues to be the mainstay of treatment for colorectal cancer. However, such major surgery for cancer is asso-

ciated with a significant level of postoperative complication and morbidity (Ghaferi et al., 2011). It has been increasingly recognised that these postoperative complications may not only have negative implications for short term outcome but also for oncologic outcomes (Law et al., 2007a,b; Mirzenami et al., 2011) and long-term survival (McArdle et al., 2005; Khuri et al., 2005).

Postoperative complications can be described as “deviation from the normal postoperative course” (Dindo et al., 2004). They can and

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Table 1
Type of complications: accepted definitions of infective complications.

Type	Location	Complication	Definition
Infective	SSI	Wound infection	The presence of pus in the wound either discharging spontaneously or requiring drainage
		Anastomotic leak	Anastomotic defect diagnosed radiologically, at endoscopy or laparotomy
		Intra-abdominal collection	Surgical or radiologically guided aspiration of pus from abdominal cavity
	RSI	Pneumonia	Fever above 38.5°C, or SIRS, associated with positive chest x-ray findings
		Septicaemia UTI	SIRS with positive blood culture Lower urinary tract symptoms, or fever, with positive urinalysis and/or urine culture
Non-infective	Wound	Seroma	Sterile superficial wound collection without fever or surrounding cellulitis
		Dehiscence	Deep or superficial separation of the wound without fever, pus or surrounding cellulitis
	Surgical site	Haemorrhage	Bleeding requiring radiological or operative intervention
		MI	Myocardial ischaemia causing ECG changes and raised cardiac enzymes/markers
	Vascular	Arrhythmia	New, resting ECG arrhythmia, requiring medical intervention
		VTE	Deep or pulmonary venous thrombosis with clinical symptoms, confirmed radiologically
		CVA	Persistent focal neurological deficit with radiological evidence of cerebral vascular territory infarction
	Urinary	Renal failure	Oliguria/anuria with decreasing GFR, with or without need for renal replacement therapy
		Acute urinary retention	Painful/painless anuria with inability to void requiring urinary catheterisation
	GI	Ileus	Paralytic/non-mechanical small bowel obstruction

SSI: surgical site infection, RSI: remote site infection, SIRS: systemic inflammatory response syndrome, UTI: urinary tract infection, MI: myocardial infarction, ECG: electrocardiogram, VTE: venous thromboembolism, CVA: cerebrovascular accident, GFR: glomerular filtration rate, GI: gastrointestinal.

have been classified in a number of ways. The earlier studies mainly considered the type of complication (Table 1), considering complications related to infection (Law et al., 2007a; Nespoli et al., 2004) and reporting a negative impact on long term oncologic outcome. Some further considered the site of infection (Law et al., 2007a; Khuri et al., 2005; Miki et al., 2006; Tsujimoto et al., 2010), reporting that intra-abdominal and pulmonary infective complications had a greater impact on long-term outcomes than wound infections. Many studies have focused on anastomotic leak as perhaps the most feared and best recorded complication related to colorectal surgery, a meta-analysis of which found significantly greater local recurrence and poorer cancer specific survival (Mirzenami et al., 2011). This has led some authors to attempt to define complications by severity, often as “minor” and “major” based on pre-defined diagnoses or their perceived significance (Rutegard et al., 2012). In particular, a recently developed method is to describe the severity of a complication objectively based on the action taken by the surgical team to remedy it (Dindo et al., 2004). This Clavien Dindo scale (Table 2) has become increasingly popular and has been validated across various surgical specialities, professionals and countries (Clavien et al., 2009). Initial applications in other cancer types have shown that increasingly severe complications have a negative impact on long-term outcomes (Petermann et al., 2013).

The present systematic review examines the relationship between the type and the severity of postoperative complications and long-term oncologic outcomes following surgery for colorectal cancer.

2. Methods

This systematic review of published literature was conducted with two primary areas of interest; the impact of type of complications (infective compared to non-infective complications) and the impact of severity of complications (as defined by the Clavien Dindo

Table 2
Severity of postoperative complications: the Clavien Dindo scale (Dindo et al., 2004).

Clavien Dindo grade	Description
0	No complication
1	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic and radiological interventions. Acceptable therapeutic regimens are: drugs as antiemetics, antipyretics, analgesics, diuretics, electrolytes and physiotherapy. This grade also includes wound infections opened at the bedside
2	Requiring pharmacological treatment with drugs other than such allowed for grade 1 complications
3	Requiring surgical, endoscopic or radiological intervention
4	3A Intervention not under general anaesthesia
	3B Intervention under general anaesthesia
	Life threatening complication requiring ICU management including CNS complications
	4A Single organ dysfunction (including dialysis)
5	4B Multi organ dysfunction
	Death

ICU: intensive care unit, CNS: central nervous system.

scale) on long-term outcome following surgery for colorectal cancer. There was also a secondary interest in whether both definitions were capturing the same underlying mechanistic process that was impacting long-term outcomes.

A literature search was made of the US National Library of Medicine (MEDLINE), PubMed, the Cochrane Database of Systematic Reviews (CDSR) and Web of Science (WoS) databases from inception to 22nd October 2014. The following search term was used in free text and medical subject heading (MeSH) “colorectal AND (cancer OR metastases) AND (surgery OR resection) AND (complications OR morbidity) AND ((infective OR infectious) OR (severity OR Clavien OR Dindo)) AND ((long-term AND outcome)

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