**Original Article**

# Title: Possible dose dependent effect of perioperative dexamethasone and laparoscopic surgery on the postoperative systemic inflammatory response and complications following surgery for colon cancer

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Disclosure / Financial support: None

Keywords: colon cancer, systemic inflammation, dexamethasone, steroids, surgery

Word count: 2,516

Running head: Dexamethasone, complications and survival in colonic resection

**Abstract**

Background:

Perioperative dexamethasone is associated with attenuation of the postoperative systemic inflammatory response and fewer postoperative complications following elective surgery for colorectal cancer.

This study examined the impact of different doses of dexamethasone, given to reduce postoperative nausea and vomiting (PONV) after elective colonic resection for cancer, on the postoperative Glasgow Prognostic Score (poGPS) and morbidity.

Methods:

Patients from a single centre were included if they underwent potentially curative resection of colonic cancer from 2008 to 2017 (n=480). Patients received no dexamethasone (209, 44%), or either 4mg (166, 35%), or 8mg (105, 21%), intravenously during anaesthesia, at the discretion of the anaesthetist. The postoperative Glasgow Prognostic Score (poGPS) on day 3 and 4, and complication rate at discharge were recorded.

Results:

When patients were grouped by surgical approach (open or laparoscopic) and dexamethasone dose (0mg, 4mg or 8mg), there was a statistically significant linear trend toward a lower postoperative systemic inflammatory response (day 3 poGPS) with the use of minimally invasive surgery and higher doses of dexamethasone ($p<0.001$). Furthermore, this

combination of laparoscopic surgery and higher doses of dexamethasone was significantly associated with a lower proportion of postoperative complications ($p<0.001$).

At multivariate Cox regression, dexamethasone was not significantly associated with either improved or poorer cancer specific or overall survival.

Conclusions:

Higher doses of perioperative dexamethasone are associated with greater reduction in postoperative systemic inflammation and complications following surgery for colonic cancer without negative impact on survival.

## 1.0 Introduction

Long term survival following surgery for colorectal cancer is primarily related to disease stage, however postoperative morbidity is also a negative prognostic factor [1]. These complications have a high price in terms of both health care costs, and impact on wider society, due to prolonged hospital stay and delay in return to function.

Postoperative complications have been reported to be associated with an exaggerated systemic inflammatory response following surgery for colorectal cancer [2]. The acute phase marker C-reactive protein (CRP) is increasingly recognised to be a reliable measure of this postoperative systemic inflammatory response (SIR) [3]. Postoperative CRP concentrations are now considered to be a useful, early surrogate marker for developing postoperative complications [4]. In addition, increasing evidence suggests that the postoperative SIR may have a causal influence on postoperative complications, and a negative impact on oncologic outcomes following surgery for colorectal cancer [5].

Corticosteroids are commonly administered at the induction of anaesthesia in colorectal surgery for the prevention of postoperative nausea and vomiting (PONV) [6]. A recent meta-analysis has reported that pre-operative administration of corticosteroids is associated with a reduction in the post-operative systemic inflammatory response, measured by CRP, and complications following surgery for gastrointestinal cancers [7]. A further recent randomised controlled trial (RCT) of perioperative corticosteroids in pancreatic cancer surgery reported a reduction in postoperative complications in patients given preoperative steroids [8]. In colorectal cancer surgery a recent observational study reported a significant association between dexamethasone, administered to reduce risk of PONV, and a reduction in both postoperative CRP concentrations and complications [9].

Despite this, no study has sought to detect whether a dose response relationship exists between perioperative steroids and either the postoperative systemic inflammatory response or complications. Furthermore, some concerns have been raised regarding the possibility of increased rates of disease recurrence in patients given perioperative steroids [10]. Therefore, the aims of the present study were to examine the impact of varying doses of dexamethasone given in the perioperative period to prevent PONV, on the postoperative systemic inflammatory response, complications, and survival following elective surgery for colon cancer.

## 2.0 Methods

2.1 Patients:

This was a retrospective observational study of patients with histologically confirmed colonic cancer, undergoing potentially curative resection, at a single centre from March 2008 to June 2017 were included. Those excluded from analysis were patients for whom there was no available anaesthetic record, those prescribed long term steroids, with diagnosed inflammatory conditions, with rectal cancer, who had emergency surgery, or palliative resection.

Each case was discussed at a specialist colorectal oncology multi-disciplinary team prior to and following resection. As described previously, all patients were given venous thromboprophylaxis and antibiotic prophylaxis at the induction of anaesthesia. Patients were managed according to a unit standardised perioperative care protocol, including early enteral nutrition, early postoperative mobilisation, and no routine nasogastric or peritoneal drainage. Patients were given intravenous dexamethasone, either 4mg or 8mg, at the induction of anaesthesia, to reduce the risk of significant postoperative nausea and vomiting, at the anaesthetic staff's discretion [9].

Patients were reviewed by their own surgical team on each postoperative day. Serum CRP and albumin were obtained from daily blood samples drawn as standard until the patient was discharged. The patient's surgical team arranged further investigation, and/or intervention, based on their own judgement and were not blind to serum CRP results.

2.2 Methods:

Anonymised clinicopathological data was recorded prospectively in a secure database, and was subsequently analysed. Patient demographics, TNM stage (TNM, 5th ed, AJCC), and in particular, factors known to influence the magnitude of the postoperative systemic inflammatory response; American Society of Anesthesiology (ASA) grade, body mass index (BMI), surgical approach and preoperative systemic inflammation, were recorded [11]. Retrospective review of anaesthetic records allowed the collection of data relating the use of dexamethasone at the induction of anaesthesia.

Serum concentrations of CRP (mg/L) and were measured using an autoanalyzer (Architect; Abbot Diagnostics, Maidenhead, UK) with a lower detectable limit of 0.2 mg/L, as was serum albumin (normal range 35-50g/L). The preoperative modified Glasgow Prognostic Score (mGPS: CRP ≤10 mg/L = 0. CRP > 10 mg/L and albumin ≥35 g/L = 1, CRP >10 mg/L and albumin <35 g/L = 2), was calculated in patients for whom preoperative serum CRP and albumin were available [12]. The validated Postoperative Glasgow Prognostic Score (poGPS: CRP ≤150 mg/L = 0; CRP >150 mg/L and albumin ≥25 g/L = 1; CRP >150 mg/L and albumin <25 g/L = 2) was calculated on postoperative days 3 and 4 [13].

Complications were recorded and the most severe for each patient categorised by its Clavien Dindo grade [14]. Infective complications were categorised as described previously [2].

The study was approved by the West of Scotland Research Ethics Committee, Glasgow, as part of surgical audit.

2.3 Statistical analysis:

The Chi square test for significance, and Chi square test for trend, were used to compare categorical and ordinal data. Univariate and multivariate binary logistic regression was used to characterise preoperative and operative factors associated with postoperative complications. Those variables associated with postoperative complications at a significance of $p<0.01$ were included in backward conditional multivariate model where a two sided p value $\leq 0.05$ was considered statistically significant. A priori subgroup analysis of those patients undergoing open and laparoscopic surgery separately was carried out as it is recognised to be a significant determinant of the postoperative systemic inflammatory response [11]. Univariate and multivariate Cox regression was used to analyse survival data. Thirty day mortalities and deaths during the index admission were excluded from analysis. On univariate Cox regression, those variables associated with cancer specific (CSS) or overall survival (OS) with statistical significance $p \leq 0.05$ were then included in multivariate Cox regression. This multivariate modelling used backward conditional regression where a two sided p value $\leq 0.05$ was used as the threshold for statistical significance. CSS was calculated as time from the date of surgery to that of death due to colonic cancer. Overall survival was calculated as time from the date of surgery to death due to any cause. All analyses were carried out using IBM SPSS for Windows (v24, Chicago, IL, USA).

## 3.0 Results

### 3.1 Patients:

The study included 480 patients in total, who had undergone surgery for colonic cancer with curative intent over the study period. The majority were female (264, 55%), over 65 years old (334, 70%), with node negative disease (297, 62%). 196 patients (41%) had a laparoscopic resection with the remainder having open surgery. 166 patients (35%) were given 4mg of dexamethasone, 105 patients (21%) were given 8mg of dexamethasone and the remainder (209, 44%) did not receive dexamethasone. Of all included patients, 154 (32%) went on to have adjuvant treatment following surgery. Of all included patients, 182 (38%) experienced a postoperative complication, of which 112 (23%) were classed as infective, and 40 (8%) were Clavien Dindo grade 3-5. There were 5 (1%) deaths either within 30 postoperative days or the index admission. Of all included patients 439 had preoperative CRP and albumin measured, allowing calculation of mGPS. 448 patients had CRP and albumin measured on postoperative day 3, allowing calculation of poGPS 3, and 375 patients had CRP and albumin measured on postoperative day 3, allowing calculation of poGPS 4.

### 3.2 Impact of dexamethasone in patients undergoing elective colon cancer resection:

Within the 480 included patients (Table 1) there was a significant association between perioperative dexamethasone dose received and patients ASA grade ($p=0.007$), preoperative mGPS ($p=0.003$), TNM stage ($p=0.022$), intraoperative blood transfusion ($p=0.012$), and laparoscopic surgery ($p<0.001$)

There was a significant association between perioperative dexamethasone and a lower postoperative systemic inflammatory response on postoperative days 3 (poGPS 2; 0mg 27%, 4mg 13%, 8mg 8%, p<0.001), and 4 (poGPS 2; 0mg 22%, 4mg 13%, 8mg 9%, p=0.007).

There was a significant association between perioperative dexamethasone and a lower rate of postoperative complications (0mg 48%, 4mg 31%, 8mg 29%, p<0.001), and infective complications (0mg 30%, 4mg 18%, 8mg 19%, p=0.009), but not Clavien Dindo grade 3-5 complications (p=0.121)

3.3 Factors associated with the postoperative systemic inflammatory response

At univariate binary logistic regression (Table 2), males sex (p=0.021), laparoscopic surgery (p<0.001), and perioperative dexamethasone (p<0.001) were significantly associated with day 3 poGPS. At multivariate binary logistic regression, laparoscopic surgery (OR 0.53, 95% CI 0.35-0.81, p=0.003) and dexamethasone (OR 0.44, 95% CI 0.29-0.66, p<0.001) remained independently associated with day 3 poGPS.

3.4 Factors associated with postoperative complications:

At univariate binary logistic regression (Table 2), male sex (p=0.004), ASA (p=0.007), preoperative mGPS (p=0.010), laparoscopic surgery (p<0.001), perioperative dexamethasone dose (p<0.001), intraoperative blood transfusion (p=0.013) and day 3 poGPS (p<0.001) were significantly associated with postoperative complications. At multivariate binary logistic regression, dexamethasone (OR 0.51, 95% CI 0.32-0.84, p=0.008), and day 3 poGPS (OR 2.42, 95% CI 1.76-3.33, p<0.001) remained independently associated with postoperative complications.

3.5 The magnitude of the postoperative systemic inflammatory response and complications:

When patients were grouped by surgical approach (open or laparoscopic) and dexamethasone dose (0mg, 4mg or 8mg), there was a statistically significant linear trend (Table 3) toward a lower postoperative systemic inflammatory response (day 3 poGPS) with the use of minimally invasive surgery and higher doses of dexamethasone ($p<0.001$). Furthermore, this combination of laparoscopic surgery and higher doses of dexamethasone was significantly associated with a lower proportion of postoperative complications ($p<0.001$).

3.6 Impact of dexamethasone on survival following elective colon cancer resection:

There were 136 deaths during the study period, of which 74 were due to colonic cancer. The median follow up for patients alive at the time of censoring was 55 months (range 12-122). At multivariate analysis, neither dexamethasone or grouping by surgical approach and dexamethasone dose were significantly associated with either improved or poorer cancer specific or overall survival (Table 4).

## 4.0 Discussion

The present study reports a possible dose response relationship between attenuation of the postoperative systemic inflammatory response measured by the poGPS and postoperative complications, through a combination of dexamethasone given at the induction of anaesthesia and laparoscopic surgery. Indeed, when patients were grouped by surgical approach and perioperative dexamethasone, there was a linear association between the magnitude of the surgical injury, postoperative systemic inflammatory response, and complications. Furthermore, despite prior concerns, the present study reports no association between dexamethasone and poorer oncologic outcomes.

Currently corticosteroids are primarily given in the perioperative period to reduce post-operative nausea and vomiting (PONV) [15]. The recent "Dexamethasone versus standard treatment for postoperative nausea and vomiting in gastrointestinal surgery: randomised controlled (DREAMS) trial reported a significant reduction in PONV in patients undergoing colorectal surgery given 8mg intravenous dexamethasone compared to placebo [6]. Perioperative steroids have also been shown to reduce postoperative pain, with calls to expand their use and proceed with procedure specific dose finding studies in this context [16]. A previous propensity score matched study published by our group in patients with colorectal cancer reported a significant association between dexamethasone, attenuation of the postoperative systemic inflammatory response, and fewer postoperative complications [9]. However, the present study moves the debate forward, being to our knowledge the first work to report a "dose dependent" relationship between attenuation of the postoperative systemic inflammatory response and complications. A recent Cochrane review reported no association between perioperative steroids and wound complications across a variety of surgical specialties, however, did not report the relationship with any measures of the

postoperative systemic inflammatory response [17]. Furthermore, two currently recruiting randomised controlled trials of perioperative dexamethasone, PADDI (ACTRN12614001226695) and PACMAN (NCT03218553), are investigating the effect on surgical site infection, and major postoperative complications respectively. However, neither are limited to colorectal surgery, and neither include measures of the postoperative systemic inflammatory response in their outcomes.

The mechanism of action through which dexamethasone, and other corticosteroids, have their anti-inflammatory effects have still to be completely elucidated. With regard to the adaptive immune system, amongst other effects, down regulatory effects on lymphoid tissue are thought to occur through inhibition of nuclear factor κB (NF- κB) [18]. In relation to the innate immune system, increased transcription of lipocortins leads to down-regulation of cyclo-oxygenase related pathways, whilst steroids decrease circulating pro-inflammatory mediators including IL 6, resulting in an overall lessening of this response [19-20]. Recent evidence in healthy volunteers and surgical patients given doses of dexamethasone similar to that used to prevent PONV have shown rapid effects on circulating innate immune cells and circulating cytokines and may both initially attenuate innate immune responses but then allow for later immune activation, suggesting an immunomodulatory role rather than that of straightforward immunosuppression [21-22].

Laparoscopic surgery is well recognised to be associated with a reduction in the magnitude of the postoperative systemic inflammatory response following colorectal surgery [11]. Furthermore, it has been reported to be associated with fewer postoperative complications [13]. Whether this simply relates to the smaller abdominal wounds required, or whether other factors such as the use of carbon dioxide for insufflation, or the no-touch isolation technique generally used, remains unclear.

Although postoperative complications are recognised to have a negative impact on cancer specific survival and disease recurrence, the mechanism by which they lead to these poorer outcomes is unclear [23]. The creation of a pro-metastatic environment through systemic inflammation, both in relation to surgical trauma, and as a consequence of postoperative complications, could be hypothesised to be such a mechanism, allowing metastatic disease progression [24]. It could then be hypothesised that a reduction in the magnitude of the postoperative systemic inflammatory response may improve long term outcomes following surgery for colorectal cancer through direct means and through a reduction in postoperative complications, although this could not be demonstrated with statistical significance in the present study.

The main limitation of the present study was its retrospective nature. The administration of dexamethasone, and the use of minimally invasive surgery, was entirely at the discretion of the surgical and anaesthetic team, and therefore possible bias exists with regard to individual surgeon outcomes. There were significant differences amongst the patients when grouped by dexamethasone dose, specifically with regards to the proportions of patients undergoing open or laparoscopic surgery. However, given that surgical approach is the main confounder of postoperative systemic inflammation [25], subgroup analysis was necessary. Patients who underwent open surgery and received 8mg of dexamethasone were an outlier with regard to the overall linear relationship, in that they had a relatively high rate of postoperative complications. However, they were the smallest subgroup, which may have impacted the analysis. In addition, patients undergoing rectal cancer surgery were not included as they represent a much more heterogeneous group with regards to their surgery, preoperative oncology, and anaesthesia. It is reassuring then, that the results pertaining to long term outcome are in keeping with those recently published by a group examining the use of dexamethasone in pancreatic cancer surgery [26].

## 5.0 Conclusions

The present retrospective study in patients undergoing elective surgery for colonic cancer reports a possible dose dependent reduction in the postoperative systemic inflammatory response, and fewer complications, associated with the combination of laparoscopic surgery and dexamethasone. The use of dexamethasone was not associated with any negative prognostic impact. These findings should be assessed in prospective randomised studies to allow consideration as to whether dexamethasone should be administered in this group of patients for reasons other than purely postoperative nausea and vomiting.

## Acknowledgments

We thank the surgical department and Consultant Colorectal Surgeons of Glasgow Royal Infirmary for their input.

**Conflicts of interest**

**None**

**Sources of funding**

**None**

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## Tables and footnotes

**Table 1:** Association between clinicopathological characteristics, perioperative factors and preoperative dexamethasone in patients undergoing elective surgery for colonic cancer

| Characteristic | | Preoperative dexamethasone | | | P |
|---|---|---|---|---|---|
| | | No, n (%) | 4mg, n (%) | 8mg, n (%) | |
| N | | 209 (44) | 166 (35) | 105 (21) | - |
| **Clinicopathological** | | | | | |
| Age (years) | <65 | 59 (28) | 52 (31) | 35 (33) | 0.216 |
| | 65-74 | 82 (39) | 66 (40) | 42 (40) | |
| | >74 | 68 (33) | 48 (29) | 28 (27) | |
| Sex | Male | 84 (40) | 91 (55) | 41 (40) | 0.655 |
| | Female | 125 (60) | 75 (45) | 64 (60) | |
| BMI (kg/m2) | <20 | 12 (6) | 10 (6) | 3 (3) | 0.406 |
| | 20-25 | 60 (31) | 57 (35) | 27 (26) | |
| | 26-30 | 53 (28) | 48 (30) | 38 (36) | |
| | >30 | 67 (35) | 47 (29) | 37 (35) | |
| ASA | 1 | 32 (16) | 33 (20) | 22 (22) | 0.007 |
| | 2 | 89 (43) | 74 (45) | 51 (50) | |
| | 3 | 72 (35) | 53 (33) | 27 (27) | |
| | 4 | 12 (6) | 3 (2) | 1 (1) | |
| Preop mGPS | 0 | 131 (70) | 120 (80) | 80 (82) | 0.003 |
| | 1 | 17 (9) | 14 (9) | 10 (10) | |
| | 2 | 40 (21) | 17 (11) | 8 (8) | |
| TNM stage | 1 | 34 (16) | 42 (26) | 27 (26) | 0.022 |
| | 2 | 91 (44) | 60 (37) | 43 (41) | |
| | 3 | 70 (34) | 54 (33) | 33 (32) | |
| | 4 | 12 (6) | 6 (4) | 1 (1) | |
| **Operative** | | | | | |
| Approach | Open | 161 (77) | 77 (47) | 40 (39) | <0.001 |
| | Laparoscopic | 47 (23) | 86 (53) | 63 (61) | |
| Surgery >4h | Yes | 29 (14) | 42 (26) | 19 (19) | 0.156 |
| | No | 174 (86) | 121 (74) | 83 (81) | |
| Intraop blood transfusion | Yes | 17 (10) | 4 (3) | 2 (3) | 0.012 |
| | No | 152 (90) | 126 (97) | 68 (97) | |
| **Postoperative** | | | | | |
| poGPS 3 | 0 | 83 (42) | 98 (65) | 72 (74) | <0.001 |
| | 1 | 62 (31) | 33 (22) | 17 (18) | |
| | 2 | 55 (28) | 20 (13) | 8 (8) | |
| poGPS 4 | 0 | 113 (62) | 85 (69) | 53 (76) | 0.008 |
| | 1 | 28 (16) | 23 (18) | 11 (16) | |
| | 2 | 40 (22) | 16 (13) | 6 (9) | |
| Any complication | Yes | 100 (48) | 51 (31) | 31 (29) | <0.001 |
| | No | 107 (52) | 114 (69) | 73 (71) | |
| Infective complication | Yes | 63 (30) | 29 (18) | 20 (19) | 0.009 |
| | No | 114 (70) | 136 (82) | 84 (81) | |

| | | | | | |
|---|---|---|---|---|---|
| Clavien Dindo 3-5 | Yes | 21 (10) | 14 (9) | 5 (5) | 0.121 |
| | No | 186 (90) | 150 (91) | 99 (95) | |

*BMI* body mass index. *ASA* American Society of Anesthesiologists score. *POD* postoperative day. *CRP* C-reactive protein, *mGPS* preoperative modified Glasgow Prognostic score (0 = CRP<10mg/L, 1 = CRP≥10mg/L and albumin ≥35g/L, 2 = CRP≥10mg/L and albumin <35g/L), poGPS postoperative Glasgow Prognostic Score (0 = CRP<150mg/L, 1 = CRP>150mg/L and albumin >25g/L, 2 = CRP>150mg/L and albumin<25g/L)

**Table 2**: Impact of preoperative dexamethasone dose on postoperative systemic inflammation and complications following surgery for colonic cancer, univariate and multivariate binary logistic regression

| **poGPS 3 ≥1** | **Univariate OR (95% CI)** | **P** | **Multivariate OR (95% CI)** | **P** |
|---|---|---|---|---|
| Age | 0.96 (0.76-1.22) | 0.754 | - | - |
| Male Sex | 1.56 (1.07-2.27) | 0.021 | 1.49 (1.00-2.21) | 0.051 |
| BMI | 1.15 (0.93-1.42) | 0.188 | - | - |
| ASA | 1.08 (0.84-1.37) | 0.574 | - | - |
| mGPS | 1.28 (0.98-1.67) | 0.073 | - | - |
| Laparoscopic | 0.41 (0.28-0.61) | <0.001 | 0.53 (0.35-0.81) | 0.003 |
| Dexamethasone (any dose) | 0.35 (0.24-0.52) | <0.001 | 0.44 (0.29-0.66) | <0.001 |
| Surgery >4h | 0.78 (0.48-1.27) | 0.320 | - | - |
| Transfusion | 1.63 (0.70-3.83) | 0.259 | - | - |
| TNM stage | 1.13 (0.90-1.42) | 0.286 | - | - |
| **Complications** | **Univariate OR (95% CI)** | **P** | **Multivariate OR (95% CI)** | **P** |
| Age | 1.15 (0.92-1.43) | 0.214 | - | - |
| Male Sex | 1.66 (1.17-2.36) | 0.004 | - | 0.182 |
| BMI | 0.95 (0.78-1.14) | 0.568 | - | - |
| ASA | 1.36 (1.09-1.71) | 0.007 | - | 0.686 |
| mGPS | 1.38 (1.08-1.77) | 0.010 | - | 0.370 |
| Laparoscopic | 0.43 (0.29-0.62) | <0.001 | - | 0.749 |
| Dexamethasone (any dose) | 0.45 (0.31-0.66) | <0.001 | 0.51 (0.32-0.84) | 0.008 |
| Surgery >4h | 1.21 (0.78-1.88) | 0.396 | - | - |
| Transfusion | 3.06 (1.26-7.43) | 0.013 | - | 0.162 |
| TNM stage | 0.93 (0.75-1.15) | 0.495 | - | - |
| poGPS 3 | 2.56 (2.01-3.27) | <0.001 | 2.42 (1.76-3.33) | <0.001 |

*OR* Odds Ratio, *CI* Confidence Interval , *BMI* body mass index. *ASA* American Society of Anesthesiologists score. *POD* postoperative day. *CRP* C-reactive protein, *mGPS* preoperative modified Glasgow Prognostic score (0 = CRP<10mg/L, 1 = CRP≥10mg/L and albumin ≥35g/L, 2 = CRP≥10mg/L and albumin <35g/L), poGPS postoperative Glasgow Prognostic Score (0 = CRP<150mg/L, 1 = CRP>150mg/L and albumin >25g/L, 2 = CRP>150mg/L and albumin<25g/L)

**Table 3:** Association between attenuation of the magnitude of the postoperative systemic inflammatory response and postoperative complications in patients undergoing elective surgery for colonic cancer

| **Characteristic** | | **Open 0mg Dex** n (%) | **Lap 0mg Dex** n (%) | **Open 4mg Dex** n (%) | **Open 8mg Dex** n (%) | **Lap 4mg Dex** n (%) | **Lap 8mg Dex** n (%) | **P** |
|---|---|---|---|---|---|---|---|---|
| N | | 161 (34) | 46 (10) | 76 (16) | 39 (8) | 84 (18) | 66 (14) | - |
| poGPS 3 | 0 | 61 (39) | 21 (49) | 41 (58) | 23 (62) | 53 (70) | 50 (82) | <0.001 |
| | 1 | 49 (31) | 13 (30) | 15 (21) | 8 (22) | 18 (24) | 9 (15) | |
| | 2 | 46 (30) | 9 (21) | 15 (21) | 6 (16) | 5 (7) | 2 (3) | |
| Complication | Yes | 81 (50) | 19 (41) | 28 (37) | 19 (48) | 22 (26) | 13 (19) | <0.001 |
| | No | 80 (50) | 27 (59) | 48 (63) | 20 (52) | 62 (74) | 53 (81) | |

*BMI* body mass index. *ASA* American Society of Anesthesiologists score. *POD* postoperative day. *CRP* C-reactive protein, *mGPS* preoperative modified Glasgow Prognostic score (0 = CRP<10mg/L, 1 = CRP≥10mg/L and albumin ≥35g/L, 2 = CRP≥10mg/L and albumin <35g/L), poGPS postoperative Glasgow Prognostic Score (0 = CRP<150mg/L, 1 = CRP>150mg/L and albumin >25g/L, 2 = CRP>150mg/L and albumin<25g/L)

**Table 4**: Impact of preoperative dexamethasone dose, postoperative systemic inflammation and complications on survival following surgery for colonic cancer, univariate and multivariate survival analysis (Feb 19)

| Survival | Variable | Univariate HR (95% CI) | P | Multivariate HR (95% CI) | P |
|---|---|---|---|---|---|
| **CSS** | Age | 1.50 (1.06-2.17) | 0.024 | 1.62 (1.12-2.33) | 0.010 |
| | Male Sex | 1.66 (0.95-2.99) | 0.075 | - | - |
| | ASA | 1.18 (0.84-1.67) | 0.336 | - | - |
| | mGPS | 1.43 (1.01-2.02) | 0.041 | - | 0.467 |
| | Laparoscopic | 0.79 (0.45-1.39) | 0.416 | - | - |
| | Dexamethasone (any dose) | 0.66 (0.38-1.12) | 0.126 | - | - |
| | Lap/Dex inflammation group | 0.89 (0.77-1.04) | 0.132 | - | - |
| | TNM stage | 2.57 (1.79-3.69) | <0.001 | 2.77 (1.89-4.06) | <0.001 |
| | poGPS 3 | 1.29 (0.93-1.79) | 0.132 | - | - |
| | Complication | 1.64 (0.97-2.79) | 0.065 | - | - |
| **OS** | Age | 1.76 (1.36-2.27) | <0.001 | 1.57 (1.19-2.09) | 0.002 |
| | Male Sex | 1.50 (1.01-2.21) | 0.043 | - | 0.132 |
| | ASA | 1.54 (1.20-1.97) | 0.001 | 1.35 (1.01-1.79) | 0.040 |
| | mGPS | 1.60 (1.26-2.03) | <0.001 | 1.34 (1.05-1.71) | 0.021 |
| | Laparoscopic | 0.72 (0.47-1.08) | 0.113 | - | - |
| | Dexamethasone (any dose) | 0.62 (0.41-0.91) | 0.016 | - | 0.918 |
| | Lap/Dex inflammation group | 0.87 (0.78-0.97) | 0.013 | - | 0.678 |
| | TNM stage | 1.76 (1.37-2.26) | <0.001 | 1.75 (1.34-2.28) | <0.001 |
| | poGPS 3 | 1.23 (0.97-1.57) | 0.095 | - | - |
| | Complication | 1.58 (1.09-2.31) | 0.017 | 1.49 (0.99-2.23) | 0.055 |

*HR* Hazard Ratio, *CI* Confidence Interval , *DSS* disease specific survival, *OS* overall survival, *mGPS* modified Glasgow Prognostic Score, *POD* postoperative day