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Research Report

Impact of steroid use and glycemic control on postoperative complications in diabetic gynecologic oncology patients undergoing laparotomy

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ABSTRACT

Objective: We aimed to assess the impact of preoperative steroid administration and perioperative glycemic control on postoperative complications in diabetic gynecologic oncology patients undergoing laparotomy.
Methods: This retrospective cohort study included gynecologic oncology patients with Type I and Type II diabetes (DM) undergoing laparotomy for any gynecologic indication at a single academic center from 10/2017 to 09/2020. The primary outcome was the rate of postoperative complications. Preoperative steroid administration and 24-hour postoperative average serum blood glucose (BG) $\geq$ 180 mg/dL were the studied exposures. Data was analyzed with SPSS Statistics v.28.
Results: 225 patients met inclusion criteria; 47.6 % had postoperative complications. Patient demographics were similar between patients with and without postoperative complications. Patients with complications had higher BMIs (36.8 vs. 34.0; $p = 0.03$), bowel surgery (33.0 % vs. 17.1 %; $p = 0.008$), operative time $\geq$ 240 min (14.2 % vs. 5.1 %; $p = 0.02$) and average BG $\geq$ 180 (63.6 % vs. 40.2 %; $p < 0.01$). On multivariate analysis, bowel surgery (OR 2.4 (1.2–4.8); $p = 0.01$) and average BG $\geq$ 180 (OR 2.8 (1.6–4.9); $p < 0.01$) remained significant predictors of postoperative complications. There were no differences in complication rates (42.3 % vs. 42.6 %; $p = 1.0$) between patients who received preoperative steroids and those who did not. When stratified by average postoperative BG < 180 mg/dL vs. BG $\geq$ 180 mg/dL, there was no difference in Clavien-Dindo classification, 30-day readmission rate (28.2 % vs. 22.1 %; $p = 0.49$) or 30-day mortality rate (2.9 % vs. 0.0 %; $p = 0.53$).
Conclusion: The administration of preoperative steroids did not increase complication rates. Perioperative hyperglycemia was associated with an increased risk of postoperative complications. Optimizing perioperative glycemic control is imperative to decrease postoperative complications.

1. Introduction

According to 2018 data from the Centers for Disease Control and Prevention (CDC), 16.2 % of women are estimated to have diabetes in the United States (National Diabetes Statistics Report, 2020). Due to this prevalence, diabetes is a common comorbidity encountered in both benign gynecologic and gynecologic oncology patient populations. Specifically, in the gynecology oncology population, diabetes has been studied as a risk factor for ovarian and endometrial cancer (Lees and Leath, 2015). Surgery is a crucial component in treating many gynecologic and gynecologic oncology conditions. It is known that diabetic patients are at increased risk for postoperative complications (Patterson, 2017; Dhatariya et al., 2012; Belmont et al., 2014). Some of these complications can be attributed to preoperative risk factors intrinsic to diabetes such as autonomic neuropathy, nephropathy and atherosclerotic disease; however, others can be attributed to postoperative hyperglycemia, which has been shown to increase wound infections and contribute to poor wound healing (Hoogwerf, 2001; Baltzis et al., 2014; Geach, 2015).

Steroids (i.e. dexamethasone) are administered to patients preoperatively in order to decrease postoperative nausea, vomiting and pain (Chen et al., 2017). While in the non-diabetic population this may not be particularly consequential, steroid administration may be harmful in diabetic patients due to reflexive hyperglycemia (Allen et al., 2020).

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However, the data surrounding administering preoperative steroids to diabetic patients is conflicting. While some studies demonstrate no increase in postoperative complications after preoperative steroids, other studies suggest an increased complication risk (Allen et al., 2020; Egan et al., 2019). There are no studies specifically looking at the effect of preoperative steroid administration on postoperative complications in diabetic gynecologic and gynecologic oncology patients.

While it is known that hyperglycemia increases postoperative complications, there is inconclusive data regarding optimal postoperative target glucose levels particularly in diabetic gynecologic patients (Hoogwerf, 2001; Baltzis et al., 2014; Geach, 2015). Some studies suggest that a target glucose of <200 mg/dL is optimal for decreasing postoperative complications while others claim that tighter glycemic control with a target glucose of < 180 mg/dL, 150–200 mg/dL or < 139 mg/dL is preferred for reducing overall morbidity and mortality (Dhatariya et al., 2012; Ambiru et al., 2008; Kao et al., 2009; van den Berghe et al., 2001; Al-Niaimi et al., 2015; American Diabetes, 2019; Sathya et al., 2013; Poldermans, 2010; Umpierrez et al., 2012; Joshi et al., 2010). Similarly, the NICE-SUGAR trial found that a target glucose < 180 mg/dL actually lowered mortality compared to tighter glycemic control < 108 mg/dL (Investigators et al., 2009). Some of these discrepancies stem from differences in study primary outcomes; however, these differences in recommendations highlight the need for more research in this area.

In this study, we sought to evaluate the effect of perioperative glucose control on postoperative complications and determine whether the administration of preoperative steroids increased postoperative complications in diabetic gynecologic oncology patients as they are commonly used in the enhanced recovery protocol for patients undergoing laparotomy.

2. Methods

This retrospective cohort study included diabetic gynecologic oncology patients undergoing laparotomy for any gynecologic indication on an enhanced recovery protocol (ERP) at a single academic institution from October 2017 to September 2020. Patients who did not carry a diagnosis of diabetes or underwent minimally invasive surgery were excluded from the study. Diabetic patients were defined as patients who carried an existing diagnosis of type I, type II diabetes, had an unknown classification of diabetes, or had an elevated HgbA1c on admission. Patients were identified using an institutional database and were established gynecologic oncology patients or transferred due to concern of malignancy or concern for surgical complexity. A sample size of 186 (93 patients per group) was needed to provide 80 % power to detect a 20 % difference in postoperative complication rate at a two-sided 5 % significance level.

Demographics, medical comorbidities per Charlson Comorbidity index, postoperative complications, 30-day hospital readmission rate and 30-day mortality were obtained from the electronic medical record. Perioperative complications were classified into groups: pulmonary, infection, ileus, deep venous thrombosis or pulmonary embolism, cerebral vascular accident, myocardial infarction, acute kidney injury, multiple complications or other complications. Complications were further categorized using the Clavien-Dindo classification system (Clavien et al., 2009). The primary outcome was complication rate in patients with average blood glucose ≥ 180 mg/dL in the first 24 hours postoperatively versus those with an average blood glucose < 180 mg/dL. Secondary outcomes included complication rates in patients who received preoperative steroids versus those who did not.

Patient demographics, clinical characteristics and outcomes of interest were summarized using descriptive statistics. Characteristics among patients with complications and without complications were compared use the independent *t*-test and Pearson's Chi-Squared test. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) Statistics version 28 (International Business Machines Corporation (IBM), Armonk, NY).

In accordance with the journal's guidelines, we will provide our data for independent analysis by a selected team by the Editorial Team for the purposes of additional data analysis or for the reproducibility of this study in other centers if such is requested. This study obtained ethics approval from an Institutional Review Board.

3. Results

There were 2,948 patient encounters identified with a total of 225 patients meeting inclusion criteria. Of the patients, 36.0 % carried benign diagnoses while 64.0 % had a gynecologic malignancy. Patients were divided into two groups: those with any complication (n = 107, 47.6 %) including pulmonary, infection, ileus, deep venous thrombosis or pulmonary embolism, cerebral vascular accident, myocardial infarction, acute kidney injury, multiple complications or other complications and those without complications (n = 118, 52.4 %). Patient demographics including age, race, BMI, Charlson Comorbidity Index and diagnoses were similar between groups (Table 1).

BMI was higher in patients who had complications (36.8 vs. 34.0; p = 0.03). There was no difference in complication rate between patients who received preoperative steroids and those who did not (42.3 % vs. 42.6 %; p = 1.0) though 41.5 % of patients who received steroids had an average BG ≥ 180 mg/dL. There was also no significant difference in complication rate between patients who had benign pathology and those

Table 1
Patient Demographics (Postoperative Complications vs. No Postoperative Complications).

	Complications (N = 107)	No Complications (N = 118)	P-value
Age (n = 225) (years, mean ± std dev)	60.4 ± 12.7	59.8 ± 11.2	0.69
Race (n = 187)			0.74
White	33 (40.2 %)	47 (44.8 %)	
Black	45 (54.9 %)	53 (50.5 %)	
Asian	1 (1.2 %)	0 (0.0 %)	
Hispanic	1 (1.2 %)	1 (1.0 %)	
Other	2 (2.4 %)	4 (3.8 %)	
Length of Stay (n = 225) (days, mean ± std dev)	5.4 ± 6.1	2.9 ± 2.2	**<0.01**
BMI (n = 225) (kg/m^2)	36.8 ± 11.2	34.0 ± 8.0	**0.03**
CCI (n = 221)			0.85
0–4	43 (41.0 %)	47 (40.5 %)	
5–8	32 (30.5 %)	39 (33.6 %)	
9–15	30 (28.6 %)	30 (25.9 %)	
Diabetes (n = 225)			0.24
Type I	24 (22.4 %)	22 (18.6 %)	
Type II	79 (73.8 %)	95 (80.5 %)	
Not specified	4 (3.7 %)	1 (0.8 %)	
HgbA1c (n = 111) (mg/dL, mean ± std dev)	7.6 ± 2.1	7.5 ± 1.7	0.74
Diagnosis (n = 211)			0.09
Benign	29 (29.9 %)	47 (41.2 %)	
Endometrial Cancer	33 (34.0 %)	22 (19.3 %)	
Ovarian Cancer	32 (33.0 %)	40 (35.1 %)	
Cervical Cancer	3 (3.0 %)	5 (4.4 %)	
Preoperative Steroids (n = 177)			1.0
Yes	52 (69.3 %)	71 (69.6 %)	
No	23 (30.7 %)	32 (30.4 %)	

who had malignant pathology (29.9 % vs. 70.1 %; p = 0.11); however, there was a trend towards a higher complication rate in patients with malignancy. The total study population had a 14.7 % 30-day readmission rate and a 1.3 % 30-day mortality rate.

Patients with an average BG ≥ 180 mg/dL were 64 % more likely to have a postoperative complication (RR 1.64, 95 % CI 1.23–2.20). The complication group was more likely to have bowel surgery performed (33 % vs. 17.1 %; p = 0.008), operative time ≥ 240 min (14.2 % vs. 5.1 %; p = 0.02), average blood glucose ≥ 180 (63.6 % vs. 40.2 %; <0.001), and 30-day Readmission (24.3 % vs. 5.9 %; p < 0.001) (Table 2).

On multivariate analysis, bowel surgery (OR 2.4 (1.2–4.8); p = 0.01) and average blood glucose ≥ 180 (OR 2.8 (1.6–4.9); p < 0.01) remained significant predictors of postoperative complications (Table 3).

Of the complications, infection was the most common (34.1 %), followed by ileus (29.3 %), AKI (23.9 %) and pulmonary issues (17.6 %). Nearly a third of patients had multiple complications. Per the Clavien-Dindo classification system, 85.9 % of complications were Grade I-II and 14.1 % were Grade III-V. Patients with postoperative complications had a 24.3 % 30-day readmission rate and 1.9 % 30-day mortality rate.

Of the patients who had complications, there was no difference in specific complication types between those who had an average postoperative glucose < 180 mg/dL and those who had an average postoperative glucose ≥ 180 mg/dL: pulmonary (1.1 vs. 15.1 %; p = 0.58), infection (43.6 % vs. 26.9 %; p = 0.12), ileus (23.1 % vs. 34.0 %; p = 0.36), DVT/PTE (2.6 % vs 13.2 %; p = 0.13), MI (0 % vs. 3.8 %; p = 0.51), AKI (15.4 % vs. 30.2 %; p = 0.14), other (7.9 % vs. 1.2 %; p = 0.14). There was no difference in grade of Clavien-Dindo complications: Grade I-II (80.0 % vs. 90.0; p = 0.22) and Grade III-V (20.0 % vs. 10.0 %; p = 0.22), 30-day readmission rate (28.2 % vs. 22.1 %; p = 0.49) or 30-day mortality rate (0.0 % vs. 2.9 %; p = 0.53) (Table 4).

Compared to patients with benign pathology, oncology patients were more likely to have AKI as a postoperative complication (8.3 % vs. 31.0 %; p = 0.05). Otherwise, there was no difference in specific complication rates. There was no difference in 30-day readmission rate (17.2 % vs. 26.9 %; p = 0.45) or 30-day mortality (0 % vs. 2.6 %; p = 1.0) between gynecologic oncology patients and benign patients with postoperative complications (Table 5).

Table 2
Intraoperative and Postoperative Findings (Postoperative Complications vs. No Postoperative Complications).

	Complications (N = 107)	No Complications (N = 118)	P-value
Pathology (n = 211)			0.11
Benign	29 (29.9 %)	47 (41.2 %)	
Malignant	68 (70.1 %)	67 (58.8 %)	
Procedure (n = 223)			**<0.01**
Lap w/out bowel	71 (67.0 %)	97 (82.9 %)	
Lap w/ bowel	35 (33.0 %)	16 (17.1 %)	
OR time (n = 223) (minutes)			0.15
<180	68 (64.2 %)	86 (73.5 %)	
≥ 180	38 (35.8 %)	31 (26.5 %)	
OR time (n = 223) (minutes)			**0.02**
< 240	91 (85.8 %)	111 (94.9 %)	
≥ 240	15 (14.2 %)	6 (5.1 %)	
Average BG 24 h Postop (n = 224)			<0.01
< 180	39 (36.4%)	70 (59.8%)	
≥ 180	68 (63.6%)	47 (40.2%)	
30 Day Readmission (n = 225)			**<0.01**
Yes	26 (24.3 %)	7 (5.9 %)	
No	81 (75.7 %)	111 (94.1 %)	
30 Day Mortality (n = 226)			0.61
Yes	2 (1.9 %)	1 (0.8 %)	
No	105 (98.1 %)	117 (99.2 %)	

Table 3
Predictors of Postoperative Complications.

	Univariate Analysis		Multivariate Analysis	
	Odds ratio	P-value	Odds Ratio	P-value
BMI (kg/m^2)	0.97 (0.94–0.99)	**0.03**	0.97 (0.94–1.0)	0.06
Laparotomy with bowel work	2.39 (1.27–4.48)	**<0.01**	2.40 (1.21–4.77)	**0.01**
OR time ≥ 240 (minutes)	3.05 (1.14–8.18)	**0.03**	2.65 (0.93–7.58)	0.07
Average BG 24 h Postop ≥ 180 (mg/dL)	2.56 (1.49–4.40)	**<0.01**	2.75 (1.56–4.87)	**<0.01**

Table 4
Complications by average postoperative blood glucose.

	Average BG < 180 (N = 39)	Average BG ≥ 180 (N = 67)	P-Value
Complications	39 (35.8 %)	67 (58.8 %)	**<0.01**
Pulmonary	8 (21.1 %)	8 (15.1 %)	0.58
Infection	17 (43.6 %)	14 (26.9 %)	0.12
Ileus	9 (23.1 %)	18 (34.0 %)	0.36
DVT/PTE	1 (2.6 %)	7 (13.2 %)	0.13
CVA	0 (0.0 %)	0 (0.0 %)	–
MI	0 (0.0 %)	2 (3.8 %)	0.51
AKI	6 (15.4 %)	16 (30.2 %)	0.14
Other	3 (7.9 %)	11 (21.2 %)	0.14
Percentage of grade of Clavien-Dindo Complications			
Grade I-II	28 (80.0 %)	45 (90.0 %)	0.22
Grade III-V	7 (20.0 %)	5 (10.0 %)	0.22
30-Day Readmission	11 (28.2 %)	15 (22.1 %)	0.49
30-Day Mortality	0 (0 %)	2 (2.9 %)	0.53

4. Discussion

4.1. Summary of main results

Diabetic patients undergoing surgery are at increased risk for postoperative complications though there is inconclusive data regarding optimal postoperative target glucose levels to decrease this risk

Table 5
Comparing postoperative complications (Benign pathology vs. Malignant pathology).

	Benign Pathology (N = 29)	Malignant Pathology (N = 68)	P-Value
Complications	29 (38.2 %)	68 (50.4 %)	0.11
Pulmonary	5 (21.7 %)	9 (15.5 %)	0.53
Infection	10 (41.7 %)	20 (35.1 %)	0.62
Ileus	6 (25.0 %)	16 (27.6 %)	1.0
DVT/PTE	0 (0.0 %)	6 (10.5 %)	0.17
CVA	0 (0.0 %)	0 (0.0 %)	–
MI	0 (0.0 %)	2 (3.4 %)	1.0
AKI	2 (8.3 %)	18 (31.0 %)	**0.05**
Other	4 (16.7 %)	9 (15.8 %)	1.0
Percentage of grade of Clavien-Dindo Complications			
Grade I-II	22 (95.7 %)	45 (83.3 %)	0.27
Grade III-V	1 (4.3 %)	9 (16.7 %)	0.27
30-Day Readmission	5 (17.2 %)	21 (26.9 %)	0.45
30-Day Mortality	0 (0 %)	2 (2.9 %)	1.0

(Patterson, 2017; Dhatariya et al., 2012; Belmont et al., 2014; Hoogwerf, 2001; Baltzis et al., 2014; Geach, 2015). We selected an average blood glucose of 180 mg/dL as our studied cut off value, as it has been suggested to decrease postoperative complication rates in several other surgical specialties (Dhatariya et al., 2012; Ambiru et al., 2008; Kao et al., 2009; van den Berghe et al., 2001; Al-Niaimi et al., 2015; American Diabetes, 2019; Sathya et al., 2013; Poldermans, 2010; Umpierrez et al., 2012; Joshi et al., 2010). In our diabetic patient population, nearly 50 % experienced at least one postoperative complication and patients with an average postoperative blood glucose $\geq$ 180 mg/dL were more likely to have a complication. The data surrounding the administration of preoperative steroids to diabetic patients is also conflicting (Allen et al., 2020; Egan et al., 2019). In this study, there was no difference in postoperative complications between patients who received preoperative steroids and patients who did not.

4.2. Results in the context of published literature

Postoperative glycemic control in diabetic patients is a focus across several different surgical specialties to decrease postoperative complications, readmission, and mortality. Although this is crucial in caring for the diabetic population, there has not been a standardized glycemic value for optimal control and patient outcomes suggested in the literature. In this study with gynecologic oncology patients undergoing laparotomy, the overall complication rate was decreased in patients with blood glucose $<$ 180 mg/dL compared to those with blood glucose $\geq$ 180 mg/dL. This is similar to previously published data in other fields showing that an average blood glucose value of $<$ 180 mg/dL has been suggested to decrease postoperative complications (Dhatariya et al., 2012; Ambiru et al., 2008; Kao et al., 2009; van den Berghe et al., 2001; Al-Niaimi et al., 2015; American Diabetes, 2019; Sathya et al., 2013; Poldermans, 2010; Umpierrez et al., 2012; Joshi et al., 2010).

While several studies have demonstrated that hyperglycemia increases the overall postoperative complication rate, outside of surgical site infection, there is limited data surrounding the incidence of other specific complications. A randomized control trial found that strict glucose control (BG $<$ 139 mg/dL), titrated by an insulin drip, in diabetic oncology patients decreased postoperative SSIs (Al-Niaimi et al., 2015). Similarly, a prospective trial of hepatobiliary patients and found that SSIs were decreased in patients with tight glycemic control, though using BG $<$ 200 mg/dL as their demarcation (Ambiru et al., 2008). In a randomized control trial, Van den Berghe et al., found that tighter glycemic control BG $<$ 110 mg/dL reduced overall mortality and sepsis. However, a recent Cochrane review which included twelve randomized control trials, did not find a difference in strict glycemic control (BG $<$ 200 mg/dL) preventing surgical site infections, acute renal failure or cardiovascular events (Kao et al., 2009). However, in our study, there was no difference in complication classification (including surgical site infections) or Clavien-Dindo Grade when stratified by BG $<$ 180 mg/dL and BG $\geq$ 180 mg/dL.

We also sought to determine whether preoperative steroids increased postoperative complications given the risk for elevated blood sugars in the diabetic population. Allen et al. found that administration of preoperative steroids was not associated with postoperative hyperglycemia and therefore suggested benefits of administration likely outweigh risks in diabetic patients, though they did not look at complication rates (Allen et al., 2020). Whereas, another study found that there was an increased rate of postoperative complications in diabetic patients who received preoperative steroids (Egan et al., 2019). In our study, there was no difference in postoperative complication rate between patients who received preoperative steroids and those who did not. However, this result may be confounded by the fact that patients who had an extremely elevated HgbA1c were less likely to get preoperative steroids.

4.3. Strengths and weaknesses

The strength of this study is that it includes patients from a tertiary care academic center with a large catchment area, and it involves a diverse group of diabetic patients including both oncologic and benign diagnoses. This study also has several limitations. As a retrospective cohort study, it may have inherent biases that come from retrospectively abstracting data, and as it was performed at a tertiary care center, complication, readmission and mortality rates may not have been completely captured if a patient represented to a local hospital. However, the medical record was examined for any communication that indicated a patient was admitted to an outside facility.

4.4. Implications for practice and future research

Postoperative complication rates were decreased in patients who had average postoperative BG $<$ 180, supporting tighter glycemic control in the postoperative period. This glycemic target was implemented in this study as it was noted to decrease postoperative complications in other fields (Dhatariya et al., 2012; Ambiru et al., 2008; Kao et al., 2009; van den Berghe et al., 2001; Al-Niaimi et al., 2015; American Diabetes, 2019; Sathya et al., 2013; Poldermans, 2010; Umpierrez et al., 2012; Joshi et al., 2010). However, further research is needed to determine the optimal glycemic value for diabetic gynecologic oncology patients that decreases their risk of postoperative complications.

5. Conclusion

Overall, patients who had postoperative complications were more likely to have an average postoperative blood glucose $\geq$ 180 mg/dL in the first 24 h after surgery. The administration of preoperative steroids did not increase the risk of postoperative complications in the diabetic patient population. This study demonstrates that optimizing postoperative glycemic control is imperative to decrease the risk of postoperative complications.

Credit authorship contribution statement

Kaitlyn Kincaid: Writing – original draft, Project administration, Investigation, Formal analysis, Data curation. **Teresa K.L. Boitano:** Writing – review & editing, Supervision, Project administration, Methodology, Conceptualization. **Matthew Scalise:** Investigation. **Samantha Patton:** Investigation. **Charles A. Leath:** Writing – review & editing. **John M. Straughn:** Writing – review & editing. **Haller J. Smith:** Writing – review & editing, Supervision, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Financial support for Charles Leath was supported in part by the UG1 CA23330. Kaitlyn Kincaid, Teresa Boitano, Matthew Scalise, Samantha Patton, John M. Straughn, and Haller Smith have nothing to disclose.

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