SURGICAL TIMING FOR BLEEDING SIGMOID COLON ADENOCARCINOMA AFTER CORONARY ARTERY BYPASS GRAFT: A DUAL CASE EXPERIENCE AND REVIEW OF LITERATURE IN PAST TWO DECADES

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Abstract

The optimal timing of noncardiac surgery (NCS) after coronary artery bypass grafting (CABG) remains inadequately elucidated in current literature. The intricate balance between advantageous oncological outcomes associated with expeditious curative resection and the potential risk of significant post-NCS cardiac events following CABG presents a complex dilemma. This study presents a retrospective analysis of two cases involving bleeding sigmoid adenocarcinoma in the context of concomitant occlusive coronary disease. Both patients underwent CABG followed by early anterior resection. Notably, no major adverse cardiac events were observed following anterior resection procedures, and patients were discharged within a week uneventfully. A comprehensive review of literature spanning two decades was undertaken to contextualize these findings. Apparent scarcity of definitive evidence underscores the necessity for more extensive and conclusive data to establish precise guidelines for the optimal timing of NCS post-CABG.

Keywords: Timing, Colorectal Surgery, Surgical Oncology, Coronary Artery Bypass, Colorectal Neoplasms

Introduction

The perioperative morbidity and mortality associated with performing early non-cardiac surgeries (NCS) after coronary revascularisation constitute a significant area of concern. There is still a lack of comprehensive data concerning the most favourable timeframe for conducting NCS subsequent to undergoing coronary artery bypass grafting (CABG). Whayne and Saha suggested that a 90-day delay after CABG may be appropriate (1). Nonetheless, the inferior oncological outcomes linked to postponed curative cancer resection need to be balanced against the potential risks of NCS following CABG.

This case report of two cases aims to present an experience of two patients who underwent early curative resection post CABG with favourable outcomes. This paper also seeks to provide a literature review of the past two decades on this matter.

Case Report

Case 1

Mr. G was a 58-year-old gentleman. He had initially presented with chest pain and dyspnoea to the emergency department. Blood pressure was 80/56 mmHg. Electrocardiogram (ECG) showed ST depression in lead V2-6 and troponin T confirmed diagnosis of NSTEMI in cardiogenic shock. Streptokinase was given and patient was supported with noradrenaline infusion. On day 3 of admission, he developed supraventricular tachycardia, and required synchronised cardioversion 150J and IV Verapamil. His ECG showed ST elevation in leads V2-6, showing acute posterior STEMI (Killip Class IV). An angiogram showed severe occlusions of the left anterior descending (LAD) coronary artery (proximal, 90%; mid, 50%), proximal circumflex (Cx) (subtotal occlusion), and right coronary artery (RCA) (proximal, 50%; mid, 90%; distal, 90%). The left main stem (LMS) artery, posterior

descending artery (PDA) and posterior left ventricular (PLV) artery were normal. Ad-hoc percutaneous coronary intervention (PCI) with balloon angioplasty was performed. On Day 10, Mr. G complained of haematochezia while on double antiplatelet. Colonoscopy and biopsy confirmed a 10 cm long segment rectosigmoid carcinoma 15 cm from the anal verge. A multidisciplinary team (MDT) discussion was held involving cardiology, cardiothoracic, oncology and colorectal surgical teams, with subsequent coronary artery bypass graft (CABG) performed a month later. He was discharged a week following CABG uneventfully. Anterior resection was later performed 5 weeks post-CABG. During the anterior resection surgery, he required inotropic support post-induction with general anaesthesia. With concerns of aggravating cardiopulmonary stress in pneumoperitoneum, the operative team did not attempt laparoscopically. Post-operatively, patient was monitored closely in the intensive care unit for one day before being weaned off from inotropic support. He was discharged on Day 6 after anterior resection with no immediate complications.

Case 2

Mr. M had presented to the emergency department with chest pain, dyspnoea and haematochezia. He was a smoker with a three-year history of ischemic heart disease and a history of admission for unstable angina. A previous angiogram had demonstrated occlusion in LAD (proximal, 90%; mid, 80%), Cx (proximal, 90%; mid, chronic total occlusion), RCA (mid, 80%; distal, 70%), PDA (80%), PLV (80%). LMS was normal. Haemoglobin was 6 g/dL on admission and ECG showed ST depression in V4-6. He was diagnosed with secondary ischemic cardiac injury due to anaemia. Colonoscopy and biopsy confirmed a bleeding sigmoid colon adenocarcinoma occupying 70% of the lumen. He had received a total of seven units of packed red cell over the course of two-weeks before being discharged with a haemoglobin level of 9 g/dL. MDT discussion was held and CABG was performed a month later. He was discharged uneventfully on day 6 post-CABG. One week post discharge, he was readmitted for symptomatic anaemia and Type II myocardial ischemia. His haemoglobin had dropped to 6.5 g/dL due to bleeding of the sigmoid tumour and he was further transfused with two more units of packed red cell. Open anterior resection was finally performed 8 weeks after CABG. Mr. M was discharged uneventfully on Day 3 post anterior resection.

Discussion

This case report, highlighting two cases, seeks to share encounters involving the timely curative oncological resection of patients post-CABG. Both cases were similar in its presentation (Table 1) and underwent NCS 6-8 weeks post-CABG. Both patients had occlusive coronary disease complicated by acute coronary events triggered by anaemia secondary to bleeding sigmoid tumour. Available literature and their supplementary materials over the past two decades on the timing of surgery for malignancies were reviewed and summarised (Table 2). Optimal timing of NCS post-CABG remains a much-disputed subject. Delayed surgical resection not only permits the progression of disease leading to worsened outcomes but also complicates existing cardiac comorbidity with anaemia induced cardiac events. However, data concerning the most favourable timeframe for major oncological NCS post-CABG is scarce.

Table 1: Summary of the two cases for comparison

	Mr. G	**Mr. M**
Age	58	54
Other comorbidity	No other known medical illness	Diabetes mellitus type II, essential hypertension, hypercholesterolemia
Eastern Cooperative Oncology Group Performance Status	1	2
Date of acute coronary syndrome	NSTEMI with cardiogenic shock, 2/6/2022	NSTEMI with cardiogenic shock, 21/1/2022
Transthoracic Echocardiogram pre-CABG	Ejection Fraction 57% (12/7/22), mild mitral regurgitation with minimal pericardial effusion at posterior wall of left ventricle 1.37cm and inferior wall 0.8cm. Normal all chambers with no clots or thrombus.	Ejection Fraction 45% (17/7/2022) moderate left ventricle function, normal all chamber, mild mitral regurgitation and tricuspid regurgitation, normal right ventricular function, minimal pericardial effusion.
Angiogram	Proximal LAD (90%), mid LAD (50%), proximal Cx (subtotal occlusion), proximal RCA (50%), mid RCA (90%), distal RCA (90%). LMS, PDA and PLV were normal. Ad-Hoc percutaneous coronary intervention performed with balloon angioplasty.	Proximal LAD (90%), mid LAD (80%), proximal Cx (90%), mid Cx (chronic total occlusion), mid RCA (80%), distal RCA (70%), PDA (80%), PLV (80%). LMS were normal.
Date of CABG	14/07/2022	19/07/2022

Table 1: Summary of the two cases for comparison (continued)

	Mr. G	Mr. M
Colonoscopy	23/6/2022 Long segment rectosigmoid tumour about 10 cm in length, 15 cm from anal verge	31/01/2022 Large tumour at sigmoid colon, 26 cm from anal verge, occupying 70% of lumen, able to transverse the area 23/6/22 Sigmoid colon tumour - biopsied with hot snare
Initial HPE	Intramucosal carcinoma with possible adjacent invasion	High grade dysplasia with focal area suggestive of adenocarcinoma
Pre-resection CEA	2.1	2.2
CT Thorax, Abdomen and Pelvis	Intussusception of rectosigmoid junction resulting from rectosigmoid tumour. No distant metastases.	Irregular intraluminal lesion at sigmoid colon causing severe luminal narrowing. No distant metastases.
Date of Anterior Resection	23/08/2022	13/09/2022
Time interval between CABG and resection surgery	41 days (5 weeks and 6 days)	57 days (8 weeks and 1 day)
Dual antiplatelet before Anterior Resection	Started on both Clopidogrel and Aspirin after CABG. Clopidogrel was withheld seven days before surgery and bridged with daily dose of low molecular weight heparin (enoxaparin) before surgery. Aspirin was continued through surgery.	Started on both Clopidogrel and Aspirin after CABG. Clopidogrel was planned to be stopped seven days before surgery and bridged with daily dose of low molecular weight heparin (enoxaparin) before surgery. However, just a week before anterior resection, had another episode or lower gastrointestinal bleeding from the sigmoid tumour with symptomatic anaemia requiring transfusion. Both antiplatelets were withheld from the episode till second day post anterior resection.
Surgery done	Open anterior resection without diversion stoma	Open anterior resection without diversion stoma
Intra-op events and Operative findings	Hypotensive after induction, requiring inotropic support. Sigmoid tumour 6cm x 4cm polypoidal lesion occupying half circumferential, multiple apical lymph node felt at mesorectal	No adverse events reported. 6x4 cm polypoidal tumour covering 1/3 of circumference with multiple mesenteric lymph node palpable.
Post-op	Post operatively admitted to intensive care unit in view of high inotropic support on noradrenaline 0.4mcg/kg/min. Titrated off inotropic support and extubated on 24/8/2022 (Day 1 post op). Had otherwise uneventful stay post operatively. Discharged on day 6.	Post operatively nursed in general ward and was uneventful. Discharged on Day 3 post anterior resection as per enhanced recovery pathway.
Resection Specimen HPE	Moderately differentiated adenocarcinoma, pT2N0(0/26) cM0, LVI and PNI-, R0 resection with clear margin.	Moderately differentiated adenocarcinoma, pT2N0(0/15) cM0, LVI and PNI-, R0 resection with clear margin.
Outcome and follow up	CEA 3 monthly surveillance, no adjuvant therapy required	CEA 3 monthly surveillance, no adjuvant therapy required
Cardiac events reported post-surgery	None in 1 year follow up.	None in 1 year follow up.

CABG: coronary artery bypass graft
CEA: carcinoembryonic antigen
CT: computed tomography
Cx: circumflex artery (coronary)
ECG: electrocardiogram
EF: ejection fraction
Hb: haemoglobin
HPE: histopathological examination
LAD: left anterior descending artery (coronary)
LMS: left main stem artery (coronary)
LV: left ventricle
LVI: lymphovascular infiltration
NSTEMI: non-ST-segment elevated myocardial infarction
PCI: percutaneous coronary intervention
PDA: posterior descending artery (coronary)
PLV: posterior left ventricular artery (coronary)
PNI: perineural invasion
RCA: right coronary artery
STEMI: ST-segment elevated myocardial infarction

Table 2: Literature review on the timing of noncardiac surgery (NCS) post-coronary artery bypass graft (CABG)

Author, Year	Study Type, Sample Population	Timing of NCS post-CABG	Outcome
Tokushige et al., 2014 (2)	Observational study, 560 patients underwent NCS after CABG; 85/560 (15%) underwent abdominal surgeries; 94/560 (17%) patients who underwent NCS after CABG have malignancy*	146/560 (26%) within 42 days	Ischemic events appeared higher among those who underwent NCS post-CABG before 42 days vs those after (4.1% vs 2.7%). Risk for ischemic outcomes after major surgery trended to be higher in the CABG group than in the PCI group but the former had a lower risk of bleeding when undergoing NCS within 42 days.
Mookadam et al., 2011 (3)	Observational study, 211 patients**	Within 1 year**	21/211 (10%) had 24 adverse events, 11 of which died within 1 year. 15/24 (62.5%) adverse events occurred in patients who had NCS within 90 days post-CABG. The length of time between CABG and NCS did not affect the rate of adverse outcomes among elective NCS patients using 30, 45, 90, or 180 days as cut-offs.
Breen et al., 2004 (4)	Observational study, 3288 patients underwent lower extremity bypass graft surgery and 921 patients underwent abdominal aortic surgery post-CABG	< 1 month (*n* = 34); 1-2 months (*n* = 23); 2-3 months (*n* = 25); > 3 months (*n* = 4127)	Mortality risk (7/34, 20.6%) was significantly higher in those undergoing vascular surgery < 1-month post-CABG compared to those undergoing vascular surgery within 1–2 months following CABG (0/23; $p = 0.014$), 2–3 months (0/25; $p = 0.017$), or all other patients' post-CABG ($p < 0.00001$). Risk of congestive heart failure, renal failure was also higher in this group
Daye et al., 2008 (5)	Observational study, 272 patients underwent 467 major NCS; 17% were abdominal surgery	Mean of 1.9 years (± 1.9 years; range: 0–7.8 years)	Major complications occurred in 3/467 NCS (0.6% [95% confidence interval, 0.1-1.9%]) (one for colon adenocarcinoma resection at 5 months post-CABG and had cardiac arrhythmia. Another two died: one after splenectomy at 0.9 years post-CABG for polycythaemia rubra vera, and another had resection of tongue cancer at 4.1 years post-CABG). 5 patients who died after NCS done during the index CABG hospitalisation were excluded from analysis.
Özsöyler et al., 2006 (6)	Case series, 10 patients (3 colorectal cancers, 2 stomach cancers, 2 breast cancers, 1 surrenal cancer, 1 laryngeal cancer, 1 meningioma)	Mean of 42.7 days***	No cardiac event was reported during the NCS post-CABG

*Number of patients who underwent surgical resection for malignancy was not specified
**Malignancy and the number of elective surgeries not specified. Mean timing of NCS not specified
***Timing of surgery for colorectal cancer not specified
CABG: coronary artery bypass graft
NCS: noncardiac surgery
PCI: percutaneous coronary intervention

Adverse events after NCS post-coronary revascularisation are not uncommon, but appeared to be time-dependent (2–4). While the literature available appeared to agree on early NCS post-CABG resulted in increased adverse outcomes, the suggested 90 days interval between CABG and subsequent NCS is conjectural (1). Mookadam et al. reported that 10% developed adverse events after NCS post-CABG, of which half of them died within a year (3). Among these, 62.5% of adverse events occurred among those who underwent NCS within 90 days post-CABG. However, when emergency operations were excluded from the analysis, the rate of adverse outcomes was not associated with the length of time interval between CABG and NCS.

A ten-year retrospective review of patients who underwent vascular surgery post-CABG revealed that 7 out of 34 (20.6%) patients died when operated on within one-month post-CABG, of which three were peripheral vascular procedures and four were abdominal aortic aneurysm surgeries (4). Risk of congestive heart failure and renal failure were significantly higher when operated within 1-month post-CABG. Another retrospective review of 272 patients who underwent NCS post-CABG had suggested a low perioperative risk of NCS post-CABG. Only 0.6% of patients had major complications, with a mean interval of 1.9 years post- CABG (5). In a large Japanese multicentre review of 14,383 patients comparing risk of NCS post-CABG and PCI, ischemic events appeared higher among those

who underwent NCS post-CABG before 42 days compared to those after (4.1% vs 2.7%), with its risk trending higher when major surgeries were undertaken post-CABG (2).

Hitherto, no consensus has been proposed for cancer patients with resectable tumour planned for curative resection. In the cases of both patients presented, the need for surgery were imminent considering the bleeding tumour was further complicated by cardiac events. A MDT discussion was held involving the Cardiothoracic Surgical Unit, Colorectal Surgical Unit, Cardiology as well as Oncology to decide on the timing and management of both cases. CABG was performed without immediate complication and NCS was performed within two months after. The first had transient hypotension immediately after induction of general anaesthesia and required inotropic support, which was weaned off the day after surgery. Both patients had otherwise recovered well after anterior resection and were discharged home with no other deviation from expected recovery. Fortunately, both patients had relatively early stage of malignant pathology, resected with curative intent and did not require adjuvant therapy. Both patients remained well with no cardiac events after one-year follow up.

Conclusion

The optimal timing of curative tumour resection following CABG continues to be a subject of debate. While more definitive data on the most appropriate timing for cancer surgery after CABG is warranted, this study suggests that early curative resection subsequent to CABG within 6–8 weeks could offer safe and favourable results, particularly for patients with bleeding resectable tumours. However, it remains crucial that the decision-making process, potential risks, and timing of such interventions are thoroughly discussed and coordinated through comprehensive multidisciplinary collaboration, in order to achieve the best possible outcome.

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Competing interests

The authors declare there is no conflict of interest.

Informed Consent

Informed consent had been obtained for the anonymous use of their clinical data.

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References

1. Whayne TF, Saha SP. Management strategies for noncardiac surgery following a coronary artery event. Curr Cardiol Rep. 2018; 20(1):3.
2. Tokushige A, Shiomi H, Morimoto T, Ono K, Furukawa Y, Nakagawa Y, *et al.* Incidence and outcome of surgical procedures after coronary artery bypass grafting compared with those after percutaneous coronary intervention: a report from the Coronary Revascularization Demonstrating Outcome Study in Kyoto PCI/CABG Registry Cohort-2. Circ Cardiovasc Interv. 2014; 7(4):482–91.
3. Mookadam F, Carpenter SD, Thota VR, Cha S, Jiamsripong P, Alharthi MS, *et al.* Risk of adverse events after coronary artery bypass graft and subsequent noncardiac surgery. Future Cardiol. 2011; 7(1):69–75.
4. Breen P, Lee JW, Pomposelli F, Park KW. Timing of high-risk vascular surgery following coronary artery bypass surgery: a 10-year experience from an academic medical centre. Anaesthesia. 2004; 59(5):422–7.
5. Daye J, Boatman D, Peters C, Varghese I, Haider A, Roesle M, *et al.* Perioperative risk of patients undergoing noncardiac surgery after coronary artery bypass surgery. J Investig Med. 2008; 56(6):878–81.
6. Özsöyler İ, Yilik L, Bozok Ş, Emrecan B, Kestellı M, Karahan N, *et al.* Off-pump coronary artery bypass surgery in patients with coronary artery disease and malign neoplasia: results of ten patients and review of the literature. Heart Vessels. 2006; 21(6):365–7.