Original Article

Predictors of peri-operative cardiac events and development of a scoring tool for patients with chronic kidney disease undergoing non-cardiac surgeries: A prospective observational multicentre study

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ABSTRACT

Background and Aims: Cardiovascular diseases are the leading causes of morbidity and mortality in chronic kidney disease (CKD) patients. Our aim was to derive predictors of cardiac morbidity, mortality, cardiac complications and to develop/validate a scoring tool in patients with CKD undergoing non-cardiac surgery. **Methods:** A prospective observational multicentre study was done on 770 patients with CKD. The primary outcome ("Event") was one or more than one of sudden cardiac death, pulmonary oedema, acute coronary syndrome, arrhythmia and 30-day mortality. Secondary outcome was hypertension and hypotension. Predictors of cardiac risk were identified. A scoring tool was developed on the 2018 dataset and was validated on the 2019 dataset. **Results:** The overall incidence of cardiac events was 290 (37.66%) whereas the incidence of major adverse cardiac and cerebrovascular events was 15.04%. Mortality due to cardiac cause was 13 (1.68%). On multivariate regression analysis, seven perioperative variables had significant association with increased risk of events: age > 65 years (P = 0.004), metabolic equivalents (METS) ≤4 ($P \leq 0.032$), emergency surgery (P =0.032), mean arterial pressure >119 (P = 0.001), echocardiographic scoring (P = 0.054), type of anaesthesia ($P \leq 0.0001$) and type of surgery (P = 0.056). Using these variables, a risk stratification tool was developed. C statistics showed favourable predictive accuracy (0.714) and the model showed good calibration. **Conclusion:** This risk scoring tool based on preoperative variables will help to predict the risk of events in high-risk CKD patients undergoing non-cardiac surgery. This will help in better counselling and optimisation.

Keywords: Cardiovascular diseases, death,sudden cardiac, perioperative care, renal insufficiency chronic, risk assessment

INTRODUCTION

Cardiovascular complications after non-cardiac surgeries are major contributors to postoperative morbidity and mortality.[1] There is an increasing incidence of diabetes mellitus (DM) and hypertension, the leading causes of chronic kidney disease (CKD) in India, and many of these patients require various non-cardiac surgeries.[2] CKD in itself is a predictor of adverse cardiovascular complications.[3] There are

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no Indian studies evaluating the relationship between stages of CKD and the occurrence of cardiovascular events in non-cardiac surgery. Over several years, multiple indices for perioperative cardiac risk have been developed, the most widely accepted being Lee's Revised Cardiac Risk Index (RCRI) and Gupta's Perioperative Risk for Myocardial Infarction or Cardiac Arrest (MICA) score.[4,5] In both these scoring tools, serum creatinine levels have been used as cut-offs for renal insufficiency. In the reconstructed RCRI, glomerular filtration rate (GFR) <45 ml/min/1.73 m^2 is used. Our study aimed to derive predictors of cardiac morbidity and mortality in patients with CKD undergoing non-cardiac surgery and to develop/validate a scoring tool for the prediction of cardiac complications.

METHODS

A prospective, observational, multicentre study in patients with CKD (GFR <60 ml/min/1.73 m^2) undergoing non-cardiac surgery was carried out for 20 months from 2018 to 2019 in tertiary care setups. The study was approved by the ethics committees of the involved institutes, and registered with the Clinical Trials Registry of India (CTRI/2018/03/012380). The study followed the principles of the Declaration of Helsinki. Written informed consent was taken from the patients. Prevalence of coronary artery disease is said to vary from younger to older age: 24% to 85%.[6] Using the formula [$n = z^2 * P (1-P)/d^2$], the number of patients to be recruited was 196-280. Based on the average number of patients who could be recruited in the three centres, a sample size of 770 was calculated.

Inclusion criteria were all patients with CKD [GFR <60 ml/min/1.73 m^2] undergoing non-cardiac surgery under anaesthesia. GFR was calculated by modification of diet in renal disease formula. Patients not consenting to the study, those lost to follow-up, those undergoing surgery under local anaesthesia and those with preoperative acute kidney injury were excluded from the study.

The primary endpoint of the study was the development of one of the major adverse cardiac and cerebrovascular events (MACCE) during surgery or up to 30 days after surgery- acute coronary syndrome (ACS) or myocardial infarction (MI), sudden cardiac death (SCD), pulmonary oedema, arrhythmia and 30-day mortality; secondary outcome events were hypotension and hypertension [Table 1].

Data on social, demographic and clinical variables were recorded [Annexure 1]. Other factors considered are the American Society of Anesthesiologists (ASA) class, preoperative functional status as reflected by metabolic equivalents (METS) before surgery, emergency surgery, whether the patient is on haemodialysis and duration of dialysis.

Preoperative echocardiography was done and the following parameters were recorded: the presence of regional wall motion abnormality, left ventricular hypertrophy (LVH), degree of left ventricular diastolic dysfunction (LVDD) and left ventricle ejection fraction (LVEF). Echocardiographic scoring was done by giving points to each of the above parameters and adding them up to create a seven-point echocardiography score [Annexure 2].[7]

Postoperative electrocardiogram, echocardiography, and estimation of serum electrolytes were done; blood transfusions required in the first 48 hours, cardiac event upto 30 days of surgery, length of hospital stay and 30 day mortality were recorded.

Table 1: Definitions of events

Events	Definitions
Cardiac arrest	The absence of cardiac rhythm or presence of abnormal cardiac rhythm that results in loss of consciousness requiring the initiation of any component of basic and/or advanced cardiac life support
ACS	Presence of one of the following: (1) documentation of electrocardiogram (ECG) changes indicative of acute myocardial infarction (MI)- (one or more of the following): (a) ST elevation or depression_1 mm in two or more contiguous leads (b) new left bundle branch (c) new Q-wave in two or more contiguous leads (2) Raised troponin levels
Sudden cardiac death	Sudden unexpected death caused by loss of heart function.
Hypotension	Fall in Systolic BP greater than or equal to 30% of baseline BP, persistent three readings 5 minutes apart
Hypertension	Increase in >30% from baseline BP, persistent three readings 5 minutes apart
Arrhythmias	ECG evidence of SVT/Atrial flutter, atrial fibrillation, bradyarrhythmias/second or third degree atrio ventricular conduction block
Congestive heart failure (Pulmonary oedema)	It usually presents with pulmonary oedema with raised pulmonary capillary wedge pressures, presenting clinically as acute onset of breathlessness, palpitations with desaturation and a fall in PaO_2 in ABG with bilateral pulmonary infiltrates, responding to fluid restriction, diuretic, oxygen administration and dialysis.

ACS- Acute coronary syndrome. BP- blood pressure. SVT- Supraventricular tachyarrhythmias. PaO_2 Partial pressure of oxygen in arterial blood; ABG- Arterial blood gas

Univariate analysis was performed. Clinical correlates of major cardiac complications were identified with a 2 × 2 Chi-square test or Fisher's exact test for categorical variables and a t test or Wilcoxon test for continuous variables. Using "Event" as a dependent variable, a logistic regression model was made. A P value <0.05 was considered significant. The risk factors predictive of cardiac complications were assessed. The final regression model was obtained with predictive factors.

Different approaches were used to test the cardiac risk index. These included: a comparison of major cardiac complication rates within risk classes in validation and derivation cohorts, finding out whether the factors were independent predictors of risk in the validation cohort, and a comparison of the areas under the receiver operating characteristic curve (ROC) for risk-prediction indices (P = 0.05).

The data were analysed using Stata 15 (StataCorp) software package and Statcraft platform (Predictive Analytics Solutions Pvt. Ltd. India). The dataset of 2018 consisting of 424 patients (derivation cohort) was used to develop the model and the dataset of 2019 (346 patients) served as the validation cohort. Estimated probabilities of 2018 and 2019 cohorts were compared using ROC to get C-statistic [discrimination]. Hosmer–Lemeshow χ^2 test was used to assess if the model is well calibrated.

The coefficients mentioned in the multivariate regression analysis were used to compute the estimated logit* and then translate this logit into the probability scale to calculate percent risk.

*Estimated probability = {[ei/(ei + 1)] × 100} for ith patient

A scoring tool was developed by inserting the appropriate coefficient estimates from the logistic regression model. In the scoring tool, values are entered as 0 and 1 for the absence or presence, respectively, of significant risk factors multiplied by the respective coefficient. In the case of continuous variables, values are entered as the coefficient. When the required input is entered, it gives a model-based percent estimate of postoperative "Event". We present a few examples of the calculated postoperative risk of events using this tool [Annexure 3].

X = −2.75 + 0.027*(age in years) + 0.109 *(echocardiography score) + 0.1.173*(Mean arterial pressure (MAP) ≥119) + 0.594*(MET <4) + 0.937* (elective/emergency=1)+-1.318(Anaesthesia=regional anaesthesia) + -1.33 (Anaesthesia = peripheral nerve block (PNB) +1.401 (surgery = open urology) +0.801 (surgery = laparoscopy) + 1.209 (surgery = orthopaedic).

RESULTS

A total of 770 patients were recruited in the study. Various variables in patients with events and non events group were looked at [Table 2]. A total of 290 patients developed 362 cardiac events [Figure 1]. The overall incidence of cardiac events was 37.66% and MACCE was 15.04%. Mortality from all causes was 21 (2.72%), of which 13 (1.68%) patients died of cardiovascular cause. Based on the time of occurrence, events were divided into three groups; intra-operative, 48 hours postoperative period and 30 days postoperative period. In the intra-operative period, 38 MACCE occurred while 20 and 58 occurred in 48 hours postoperatively and upto 30 days after surgery, respectively. Arrhythmia was the most common event in the intra-operative and 48 hours postoperative period while ACS occurred upto 30 days postoperatively. In the secondary outcomes, hypotension was seen more in the intra-operative period, while hypertension was seen in the postoperative period. The majority of events were seen in vascular access surgery (25.86%), high-risk endourology surgery (16.89%) and orthopaedics surgery (8.96%).

On multivariate regression analysis, seven preoperative variables had a significant association with the development of events [Table 3 and Annexure 4]. Variables were increasing age, echocardiographic score, MAP >119, METS ≤4, emergency surgery, type of surgery (open urology surgery, laparoscopic and orthopaedic surgeries) and type of anaesthesia technique.

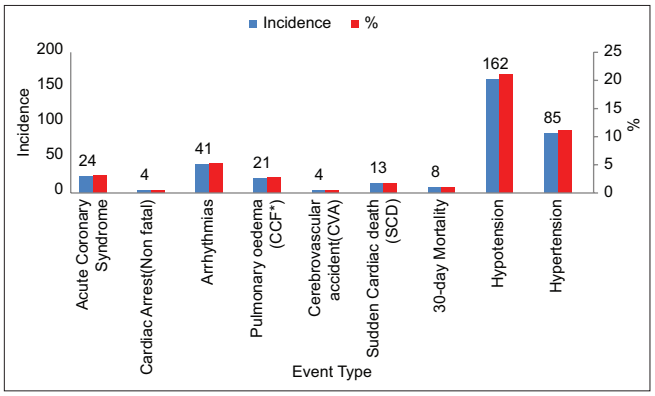

Figure 1: Type and incidence of Events

Table 2: Various Demographic and clinical parameters in event and non event group patients

Variable	All Patients (*n*=770)	%of *n*	Event (*n*=290, %)	No event (*n*=480, %)	*P*
Age in years					
<65	471	61.1	159 (54.82)	312 (65)	0.026
>65	299	38.83	131 (45.17)	168 (35)	
Gender					
Male	536	69.61	206 (71.03)	330 (68.75)	0.592
Female	234	30.38	84 (28.96)	150 (31.25)	
Smoking					
Yes	178	23.11	60 (20.68)	118 (24.58)	0.24
No	592	76.88	230 (79.31)	362 (71.41)	
History of Diabetes Mellitus					
Yes	462	60	187 (64.48)	275 (57.29)	0.050
No	308	40	103 (35.51)	205 (42.70)	
Insulin					
Yes	275	35.71	115 (39.65)	160 (33.33)	0.47
No	187		72 (24.820	115 (23.95)	
Duration of Diabetes in years			18 (SD 9)	16(SD 9)	0.384
History of Hypertension					
Yes	665	86.36	254 (87.58)	411 (85.62)	0.588
No	105	13.63	36 (12.41)	69 (14.37)	
Duration of Hypertension in years			11(SD0.9)	9.4(SD 8)	0.061
History of IHD					
Yes	174	22.59	76 (26.20)	98 (20.41)	0.103
No	596		214 (73.79)	382 (79.58)	
CKD					
Stage3	258	33.50	90 (31.03)	168 (35)	0.47
Stage4	121	15.71	52 (17.93)	69 (14.37)	
Stage5	129	16.75	51 (17.580	78 (16.25)	
Stage5D	262	34.02	97 (33.44)	165 (34.37)	
Dialysis					
Yes	262	34.02	97 (33.44)	165	0.96
Duration of Dialysis in months			17.09(SD26.75)	11.43(SD16.84)	0.45
Cerebrovascular accident					
Yes	58	7.53	29 (10)	29 (6.04)	0.031
No	712		261 (90)	451 (93.95)	
Beta blocker					
Yes	414	53.76	175 (60.30)	239 (49.79)	0.006
Aspirin					
Yes	369	47.92	151 (52.06)	218 (45.41)	0.069
Statins					
Yes	400	51.94	165 (56.89)	235 (48.95)	0.035
Clopidogrel					
Yes	115	14.93	56 (19.31)	59 (12.29)	0.007
ARB/ACE Inhibitors					
Yes	135	17.53	49 (16.89)	86 (17.91)	0.744
METS (missing 7)					
<4& =4	498	64.67	218 (75.17)	280 (58.33)	<.0001
>4	265	34.41	69 (23.79)	196 (40.83)	
Mean Arterial Pressure					
<119	491	63.76	119 (41.03)	372 (77.5)	0.006
>119	199	25.84	91 (31.37)	108 (22.5)	
Regional wall motion Abnormality					
Yes	119	15.45	62 (21.37)	57 (11.87)	<0.001
No	651	84.54	228 (78.62)	423 (88.12)	
Left Ventricular Hypertrophy					
Yes	471	61.16	190 (65.51)	281 (58.54)	0.057
No	299	38.83	100 (34.48)	199 (41.45)	

Contd...

Table 2: Contd...					
Variable	**All Patients (*n*=770)**	**%of *n***	**Event (*n*=290, %)**	**No event (*n*=480, %)**	***P***
Ejection Fraction (missing 2)					
<40	58	7.53	32 (11.03)	26 (5.41)	0.001
40-49	37	4.80	22 (7.58)	15 (3.12)	
>50	673	87.4	234 (80.68)	439 (91.45)	
Left Ventricular Diastolic Dysfunction (missing 7)					
0	162	21.03	44 (15.17)	118 (24.58)	0.046
1	536	69.61	212 (73.10)	324 (67.50)	
2	56	7.27	27 (9.31)	29 (6.04)	
3	9	1.16	4 (1.37)	5 (1.04)	
ASA Grade					
3	655	85.06	230 (79.31)	425 (88.54)	0.004
3E	50	6.49	25 (8.62)	25 (5.20)	
4	45	5.84	20 (6.89)	25 (5.20)	
4E	20	2.59	15 (5.17)	5 (1.04)	
Elective	700	90.90	248 (85.51)	452 (94.16)	<0.001
Emergency	70	9.09	42 (14.48)	28 (5.83)	
Type of Anaesthesia					
General Anaesthesia	272	35.32	126 (43.44)	146 (30.41)	0.002
Neuraxial block	217	28.18	64 (22.06)	153 (31.87)	
IV Sedation	114	14.80	41 (14.13)	73 (15.20)	
Peripheral Nerve block	167	21.68	59 (20.34)	108 (22.50)	
Type of Surgery					
Low Risk Endourology	161	20.90	55 (19.31)	106 (22.08)	0.0562
High Risk Endourology	145	18.83	49 (16.89)	96 (20)	
Vascular Access surgery	217	28.18	75 (25.86)	142 (29.58)	
Open Urological procedures	39	5.06	19 (6.55)	20 (4.16)	
Laparoscopic surgeries	28	3.63	17 (5.86)	11 (2.29)	
General Surgery	40	5.19	17 (5.86)	23 (4.79)	
Gynaecological Surgeries	10	1.29	2 (0.68)	8 (1.66)	
Orthopaedic surgeries	53	6.88	26 (8.96)	32 (6.66)	
High Risk Open Urological Surgeries	60	7.79	22 (7.58)	38 (7.91)	
Spine and Neuro surgeries	17	2.20	8 (2.75)	9 (1.87)	
Blood Transfusion	54	7.01	35 (12.06)	19 (3.95)	0.0002
Pre-operative Haemoglobin			10.45(SD2.05)	10.77(SD2.04)	0.175
Serum Creatinine			4.32(SD2.82)	4.59(SD 3.37)	0.245
Serum Potassium			4.56 (SD 0.75)	4.60(SD0.69)	0.441
Serum Bicarbonate			22.27(SD3.80)	21.96(SD 3.87)	0.281
Serum Albumin			2.98(SD 0.72)	3.25 (SD 1.15)	<0.001
Duration of Surgery in minutes			139.93(SD106.27)	120.48(SD84.36)	0.005
Length of Stay (LOS)			6 (25-75)	4 (25-75)	0.00034

n- Number of patients, *P*=<0.05 is significant. IHD- Ischaemic heart Disease; CKD- Chronic kidney disease. ARB/ACE Inhibitors- Angiotensin II Receptor Blocker/ Angiotensin converting enzyme inhibitors; ASA- American Society of Anesthesiologists

For surgery, regional and PNB proved to be beneficial as compared to general anaesthesia. Patients who developed events had a higher requirement for blood transfusion ($P = 0.0002$), longer duration of surgery ($P = 0.005$) and longer length of stay.

The estimated probabilities of 2018 and 2019 cohorts were compared by using ROC to get C-statistic [discrimination]. The C-statistic for the 2018 and 2019 cohort was 0.7641 and 0.7241 respectively [Figure 2a and b]. C-statistic showed favourable predictive accuracy and model showed good calibration (Hosmer–Lemeshow $\chi^2 = 0{\cdot}4928$, $P = 0.226$) [Table 4] in validation cohort.

DISCUSSION

As more patients with CKD undergo surgeries and cardiovascular complications are major contributors to morbidity and mortality, we need to have effective strategies and risk assessment tools for better perioperative outcomes. The current study is one of the few large cohort studies in patients with CKD (GFR <60 ml/min/1.73 m^2) to analyse predictors of cardiac events and to develop a risk scoring tool

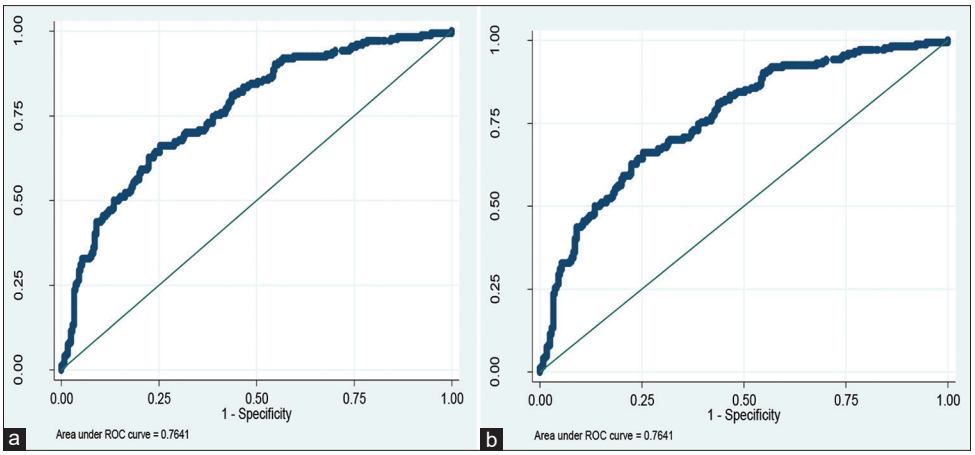

Figure 2: (a) ROC curve for Derivation cohort (2018). (b) ROC curve for Validation cohort (2019) ROC - Receiver Operating Characteristic

Table 3: Multivariate Logistic regression model of seven variables [Event as dependent variable] for Derivation cohort (2018 data)

Variables	Odds ratio	Std error	Coefficients	Z	95% CI for Odds Ratio	*P*
Age (years)	1.023	0.009	0.027	2.84	1.008-1.0046	0.004
Echo score	1.199	0.109	0.180	1.93	0.910-1.439	0.054
Mean Arterial pressure						
≤119	Ref					
>119	3.23	1.061	1.173	3.57	1.595-6.15	0.0001
METS						
>4	Ref					
<4	1.810	0.507	0.594	2.12	1.046-3.133	0.034
4	1.712	0.495	0.538	1.86	0.971-3.171	0.063
EL/EMR	2.55	1.116	0.937	2.03	1.083-6.014	0.032
Anaesthesia						
GA	Ref					
RA	0.268	0.95	-1.318	-3.73	0.134-0.535	<.0001
PNB	0.263	0.139	-1.33	-2.53	0.093-0.740	0.011
IV sedation	0.483	0.210	-0.728	-1.67	0.205-1.134	0.095
Type of Surgery						
Low risk Endourology	Ref					
High risk Endourology	1.174	0.466	0.076	0.40	0.539-2.555	0.686 ns
Vascular Access surgery	1.1127	0.412	0.630	0.29	0.538-2.30	0.773 ns
Open Urology	5.154	2.1	1.401	3.37	1.996-13.37	0.001
Laparoscopic	4.206	2.50	0.801	2.34	1.27-14.64	0.019
General surgery	2.80	2.69	1.09	1.88	0.955-8.240	0.061 ns
Gynaecology	0.232	1.54	-2.098	1.23	0.022-2.404	0.221 ns
Orthopaedic Surgery	2.362	0.276	1.209	1.91	0.977-5.979	0.055 M
High risk open Urology	2.042	1.063	0.099	1.37	0.733-0.769	0.172 ns
Spine/Neuro	2.497	1.067	0.234	1.44	0.718-8.55	0.151 ns
Constant	0.042	1.57	-2.75	-4.90	-4.431-1.898	<.0001

EL- elective surgery; EMR- Emergency surgery; GA- General anaesthesia; RA- Regional anaesthesia; PNB- Peripheral nerve block; CI- Confidence interval; Echo score-Echocardiographic Score- based on echocardiography findings (Details in Annexure 2); METS- Metabolic Equivalents; IV: Intravenous. Type of surgery –Coding details in Annexure 4

for these patients. The overall incidence of cardiac events (37.66%) in this study and MACCE (15.04%) across various non-cardiac surgeries is higher than that reported in the literature.[3-5,8] All cause mortality was 2.72%. Every sixth patient who developed MACCE died within 30 days post-surgery. The most common cause of noncardiac death was sepsis. Most deaths were seen after vascular access (6) and orthopaedic surgeries (5). Evidence shows a higher incidence of postoperative mortality in patients once the GFR drops below 60 ml/min/1.73 m^2.[9] We found no statistically significant difference in the 30 day mortality between dialysis and non-dialysis group though patients on haemodialysis were 1.56 times more at risk of

Table 4: Hosmer-Lemeshow Goodness of fit Test

Hosmer-Lemeshow Goodness of fit Test			
X squared	**df**	***P***	**Data set**
7.412166	8	0.492884	Derivation cohort
10.57983	8	0.226661	Validation cohort
10.28771	8	0.24541	Full data set

df- Degree of freedom

developing cardiac events[10] though they underwent dialysis on the previous day of surgery. We were unable to show a drop in GFR <45 ml/min/1.73 m^2 to be significantly associated with increased incidence of MACCE,[9] because our study was a cohort of CKD patients only.

We found seven preoperative variables as predictors of cardiac risk. Three of the risk factors- age, effort tolerance (METS) and type of surgery have been described earlier.[4,5] Our tool additionally included MAP, echocardiographic scoring, type of anaesthesia and emergency surgery. We could prove surgery-specific risk as published by some authors.[11] In our study, open urological procedures (9.8%), laparoscopic surgeries (5.6%), orthopaedic surgeries (8.1%) $P = 0.027$ and patients undergoing emergency surgeries ($P = 0.001$) were at a significantly higher risk of developing events. The incidence of 3.11% ACS fell within the reported range of 0.65%-6.28%.[5,10,12] All patients who developed ACS in the study had a GFR <45 ml ($P = 0.002$). Most cases of ACS (17) were seen in the postoperative period. Out of 24 patients who developed ACS, 12 required intervention. The study results showed that patients with previous percutaneous coronary intervention were 1.74 times at more risk of developing events.[13] Perioperative hypertension, LVH, changes in coagulation, ischaemic imbalance and inflammatory response may be the causes of perioperative ACS. Preoperative use of beta-blockers, aspirin and statins proved to be significantly beneficial for not developing events. Preoperatively, only fifty percent were on these cardioprotective drugs, which stresses the need for standardised preoperative care for this cohort of patients. In our study, the incidence of non-fatal cardiac arrest was 0.51% compared to 0.8% reported by Gupta and colleagues.[5] Arrhythmias in our study contributed to 5.32% of events, the most common arrhythmia being atrial fibrillation which was similar to Sellers and colleagues.[14] In CKD, hypokalemia and hyperkalemia contribute to the increased incidence of arrhythmias and MACE.[15] A prolonged inter-dialytic period predisposes these patients to SCD and arrhythmias.[16] All our patients had ASA physical status III and above (predictor of postoperative adverse cardiovascular events) but patients with ASA physical status IV (12%, $P \leq .0001$) were at a significantly higher risk of developing events.[5] A higher incidence of cardiac events with general anaesthesia in our study could be due to the presence of comorbidities and the most high risk surgeries being performed under general anaesthesia. There also was a significant association between poor effort tolerance (METS) and cardiac events.[17]

Fayad and colleagues[18] found that patients with LVDD were prone to develop MACCE and significant intra-op hypotension. In the current study, we were able to prove LVDD as a predictor of cardiac risk ($P = 0.046$). In our study, 61.6% of patients had LVH which is an important risk factor for adverse cardiovascular outcomes in patients with CKD.[19] There is a close relationship between blood pressure and perioperative outcomes. MAP variability is associated with 30-day post-operative mortality in patients undergoing non-cardiac surgery.[20] Walsh[21] in their study has shown that transient low MAP is associated with cardiac events. Low MAP is associated with raised troponin levels which is a biomarker of myocardial injury[22]; nevertheless, in our study, we did not measure troponin levels for all our patients, which would have led to an underestimation of adverse cardiac events.

Out of 21 (2.72%) patients who developed pulmonary oedema in our study, seven required noninvasive ventilation; the rest were managed with diuretics and emergency haemodialysis. Patients with preoperative diastolic dysfunction are more prone to develop postoperative pulmonary oedema, and in our study, 77.6% of patients had diastolic dysfunction.[18] Nonetheless, an association is said to exist between GFR and postoperative pulmonary complications.[23]

Hypotension and hypertension were secondary outcomes in our study with an incidence of 21.03% and 11.03% respectively. There is said to be a proportionate increase in events with increasing severity of hypotension.[24] Our patients with hypotension were taking more angiotensin-converting enzyme (ACE) inhibitors/angiotensin II receptor blockers (ARBs), as compared to patients with no hypotension ($P = 0.041$) consistent with a study published.[25] ACE inhibitors/ARBs were withheld on the day of surgery in the current study. General anaesthesia and surgical factors can lead

to hypotension during surgery.[26] Myocardial injury and death are associated with intraoperative hypotension.[26] Also, MAP >119mmHg was significantly associated with events and more so in patients on a higher number of antihypertensive medications (P = 0.029). Nevertheless, though hypotension and hypertension are not considered as MACCE, they are said to have a definite bearing on MACCE in the perioperative period.[27]

Our cohort of patients with events had a higher requirement of blood transfusions (P =0.0002) due to the presence of anaemia/or increased bleeding due to coagulation dysfunction. Low albumin levels (<3 gm %) in patients with CKD were associated with events (P = 0.001) due to poor nutritional status and inflammatory responses.

We developed a simple scoring tool and a percent risk calculator based on the 2018 data set and validated it on the 2019 data set. The scoring tool uses all preoperative variables (from multivariate analysis) which are objective and easily recordable factors associated with events in various surgical settings. Three of our factors are similar to those in the widely used Gupta's risk calculator[5] (age, METS, type of surgery). However, in the validation models, age, open urology and orthopaedic surgery did not show an association with a cardiac event. There is the possibility of getting few results slightly different in different cohorts.

Ours is the only scoring tool specifically developed for patients with CKD and which considers preoperative MAP and echocardiographic scores for calculating risk. A systematic review of all cardiac risk prediction indices showed a history of congestive heart failure, type of surgery, DM, emergency surgery, elevated creatinine and history of stroke as important risk factors.[28] Amongst these, only type of surgery and emergency surgery are included in our scoring tool. A recent systematic review of various available cardiac risk indices concluded that no single risk index gives correct prediction and we need to use two types of scoring tools to estimate cardiac risk in non-cardiac surgery.[28] Perioperative risk prediction models are significant in today's scenario as there is an emphasis on perioperative quality improvement strategies for better perioperative outcomes.[29]

The current study has some limitations. Two centres in which the study was conducted are a single speciality, and only one centre is multispeciality, where various speciality surgeries are conducted. Hence, the tool needs to be validated in a multidisciplinary setting with a larger sample. Also, we did not measure cardiac biomarkers for all patients in the study, and this must have resulted in under-estimation of silent cardiac events.[30]

CONCLUSION

With the increasing global load of the CKD population and more number of patients undergoing non- cardiac surgery, there is a higher incidence of perioperative cardiac complications. CKD being a single organ disease manifesting as total body disease, predisposes these patients to adverse perioperative outcomes. Using predictive risk scores that require a tailored approach and team effort will help deliver quality perioperative care. It is suggested that the scoring tool developed in this study can be further validated in multispeciality setups and larger populations.

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Conflicts of interest

There are no conflicts of interest.

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Annexure 1: List of Demographic and clinical variables
Age
Sex
Height
Weight
BMI
Hospital Number
Diabetes mellitus (DM)
Duration of DM (in years)
No. Of OHAs/Insulin
Hypertension (HT)
Duration of HT in years
No. Of Antihypertensives
ACE Inhibitor/ARB
Beta Blocker
Aspirin
Clopidogrel
Statins
Pre-op Systolic BP
Pre-op Diastolic BP
Pre-op Mean Arterial Pressure
Ischaemic Heart Disease
ECG
2-D Echocardiography
Regional Wall Motion Abnormality
Left Ventricular Hypertrophy
Left Ventricular Diastolic Dysfunction Grade
Ejection Fraction (%)
Cerebrovascular Accident
MDRD Glomerular filtration rate (ml/min/1.73 m^2)
CKD stage
History of congestive cardiac failure
Other co-morbidity
Smoker
Serum Creatinine
Serum Sodium
Serum Potassium
Serum bicarbonate
Serum Albumin
Dialysis (Yes/No)
Duration of Dialysis in months
Pre-op Haemoglobin
METS
HbA1c
ASA Physical status Grade
Elective/Emergency Surgery
Type of Surgery
Anaesthesia Technique
Duration of surgery in minutes
Lee's Risk Score
History of Myocardial Infarction
History of positive exercise tolerance test
Gupta's perioperative cardiac risk %
Intra-operative events
No. Of Blood Transfusions in 24 hours
Post-op 48 hrs
MDRD GFR (ml/min/1.73 m^2)
Serum Creatinine levels (Post-op) in mg%

Contd...

Annexure 1: Contd...
Serum Sodium
Serum Potassium
Serum Bicarbonate
Stage of Chronic kidney disease
2-D Echocardiography (Screening)
ECG Post operative
30 day mortality
Length of Stay (LOS) in Days
Systolic BP
Diastolic BP
Mean Arterial Pressure
Hypotension
Other complications
Sudden cardiac death
Pulmonary oedema

BP:Blood pressure;ACE:Angiotensin converting enzyme;ARB:Angiotensin receptor blocker;BMI:Body mass index;ECG:Electrocardiogram;CKD:Chronic kidney disease; MDRD:Modification of diet in renal disease;METS:Metabolic equivalents;ASA:American Society of Anesthesiologists;Pre-op:Preoperative; Post-op:Postoperative; No.=Number

Annexure 2: Echocardiographic scoring

Echo Scoring

Parameter	Score
>50	0
EF	
40-50	1
<40	2
LVH	
Y	1
N	0
RWMA	
Y	1
N	0
LVDD Grade	
0	0
1	1
2	2
3	3

EF- left ventricular ejection fraction. LVH- left ventricular hypertrophy. RWMA- Regional wall motion abnormality. LVDD- Left ventricular diastolic dysfunction. Note- Echo scoring was done based on similar type of echo scoring done in one of the published studies.[7]

Annexure 3: Calculation of Percent risk of developing events with Scoring Tool

Study_id	Age	MAP	MAP119	MET123	ELEMR	Surgerycode	Eco	Event	Anesthesia	Age_b1=0.027	MAP119_b2=1.173	MET1_b3=0.594	ELEMR_b4=0.937
-	-	-	-	-	-	-	-	-	-	0.027	1.173	0.594	0.937
S101012019	65	100	1	1	0	3	1	1	3	1.755	0	0.594	0
S102012019	67	120	2	3	0	3	4	0	3	1.809	1.173	0	0
S103012019	65	110	1	1	0	3	2	1	3	1.755	0	0.594	0
S203012019	68	140	2	2	0	3	1	0	3	1.836	1.173	0	0
S104012019	81	130	2	2	0	2	2	0	2	2.187	1.173	0	0
S107012019	62	154	2	1	0	7	2	1	1	1.674	1.173	0.594	0
S207012019	76	133	2	3	0	2	2	0	2	2.052	1.173	0	0

Study_id	Surg4_b5=1.40	Surg5_b5=1.80	Surg8_b5=1.21	Echo_b6=0.193	Anest2_b7=-1.32	Anest3_b7=-1.33	const=-2.75	Sum (L3 to v3)	Exp (w3)	X+1	X/Y	Risk %
-	1.4	1.8	1.21	0.193	-	-	-2.75	-	-	-	-	-
S101012019	0	0	0	0.193	0	-1.33	-2.75	-1.538	0.21481	1.21481	0.176826	16
S102012019	0	0	0	0.772	0	-1.33	-2.75	-0.326	0.721805	1.721805	0.419214	40
S103012019	0	0	0	0.386	0	-1.33	-2.75	-1.345	0.26054	1.26054	0.206689	20
S203012019	0	0	0	0.193	0	-1.33	-2.75	-0.878	0.415613	1.415613	0.293592	28
S104012019	0	0	0	0.386	-1.32	0	-2.75	-0.324	0.72325	1.72325	0.419701	40
S107012019	0	0	0	0.386	0	0	-2.75	1.077	2.935859	3.935859	0.745926	74
S207012019	0	0	0	0.386	-1.32	0	-2.75	-0.459	0.631915	1.631915	0.387223	38

ANNEXURE 4: CODING FOR SURGERIES

1. Low Risk Endourological procedures- Cystoscopy, Cystoscopy ureteric Stenting, cystoscopy ureteric Stent exchange, Ureterorenoscopy, Percutaneous nephrostomy, Cystoscopy with Botox injection into urethral sphincter/bladder, Transurethral bladder neck incision
2. High Risk Endourological procedures- Retrograde intra-renoscopy (RIRS), Bilateral RIRS, Percutaneous nephrolithomy, Transurethral resection of Prostate, Transurethral resection of bladder tumour
3. Vascular Access Surgery-Arteriovenous fistula (AVF) for vascular access, Arteriovenous fistula Superficialisation, Arteriovenous Graft, Tunnelled catheter placement,
4. Open urology surgery- Nephrectomy, pyeloplasty, Renal fossa exploration, Continuous ambulatory Peritoneal Dialysis catheter insertion with Omentectomy, Penile implant, Buccal mucosal graft urethroplasty, orchidectomy, scrotal exploration, radical nephrectomy, nephroureterectomy, Partial Penectomy, Partial nephrectomy
5. Laparoscopic surgeries- Laparoscopic Nephrectomy, Laparoscopic pyeloplasty, laparoscopic cholecystectomy, laparoscopic appendecectomy, laparoscopic Nephroureterectomy, laparoscopic salpingo-oopherectomy,
6. General Surgery- Hernia repair, cholecystectomy, Incision and drainage, exploratory laparotomy, Breast lump excision, mastectomy
7. Gynaecologic Surgery- Dilatation and Curettage, Hysterectomy, Ovum pick up, Ovarian cystectomy, Wertheim hysterectomy
8. Orthopaedics Surgery- Tension band wiring, Tendoachilles repair, Dynamic hip screw plating, Radial head excision, Total knee replacement, hemi hip arthroplasty, Shoulder Arthroscopy
9. High Risk open urological procedures- Renal Transplant, Radical Cystectomy, Radical Prostatectomy
10. Spine and neurosurgery- Lumbar spine decompression, Cervical spine fixation, Ventriculo peritoneal Shunt, Cerebrospinal fluid leak closure, craniotomy, lumbar discectomy

Foot note- Coding of various surgeries was done

1. Speciality
2. Authors 15 + years experience in Nephro-urology tertiary care centre