

Thromboembolic and bleeding complications in patients with prosthetic heart valves at the Kenyatta National Hospital

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Abstract

Background: Despite constant monitoring of anticoagulation in prosthetic valve patients, haematologic complications occur. This study documented the occurrence of such complications and associated risk factors at the Kenyatta National Hospital (KNH).

Study design: Observational study reviewing 142 patients, 39 prospective and 103 retrospective.

Outcome measures: International Normalised Ratio (INR); presence of signs and symptoms of haematological complications.

Results: Forty four (31%) patients presented with bleeding tendencies, 28 grade I and 4 grade III. The most common thromboembolic complication was headache in 33 (23.2%) patients.

Mean duration of anticoagulation for patients with complications was 82.9 months (\pm 64), compared to 60.8 months (\pm 43.8) in those without.

Nine patients were non-compliant in taking medications, haematologic complications presenting in 8 of them.

Conclusion: A positive association was established between haematologic complications and INR levels, duration of anticoagulation therapy, non-compliance in taking of medications, and increased period between clinic visits.

Of these only the duration of anticoagulation was an independent predictor for haematological complications.

Introduction

Since the first valve replacement, and many modifications since in valves design and surgical techniques, the recurrent problems of anticoagulant related complications continue. Complications are not without risk and can be fatal. This study documented the occurrence of haematologic complications in prosthetic valve patients at the KNH, and risk factors to their occurrence.

Patients and Methods

The study examined prosthetic heart valve patients on outpatient follow up at the KNH. The prospective arm of the study covered 16th July 2010 to 14th January 2011, the retrospective arm 10 years prior to July 21st 2010. Bioprosthetic valves were not included in the study.

Outcome measures were INR results during clinic visits, and development of complications. Complications were signs and symptoms of bleeding tendencies, neurological deficits suggestive of thromboembolism for instance fainting episodes, headaches, and dizziness (Table 1). Target INR for these patients was 2.5 – 4.5.

Data collected was analysed using STATA version 11 for

relationship using bivariate analysis and multivariate analysis for independent predictors of haematological complications. A p value of less than 0.05 was considered significant.

Results

A hundred and forty two patients were enrolled into the study, 39 prospectively and 103 retrospective. Sixty one percent of patients were female. Thirty three percent of the patients had at least a basic education and 21% in formal employment (table 2).

Most common surgery was mitral valve replacement and an almost equal number of aortic and double valve replacement surgeries (table 3).

More than half the patients returned to the outpatient clinic within 3 months of their previous visit.

Mean INR level for study population was 2.3 ± 0.7 . In the prospective arm of the study, 13 patients reported noncompliance or interruption in taking medication for various reasons including dental procedures, during menses, elevated INR and pregnancy.

A total of 78 (54.9%) patients developed haematological complications, of these 20 had both thrombotic and

Table 1: Definition of complications

Thrombo-embolism	Grade I	Grade II	Grade III
	Questionable events (e.g. dizziness) not requiring medical treatment.	Complaints presumably connected with on-going anticoagulation, requiring outpatient treatment and causing no lasting impediments (including transient ischemic attacks).	Prosthetic thrombosis requiring inpatient treatment and causing long-term impediments.
Bleeding	Mild bleeding (e.g. of the gums) not requiring medical treatment.	Haemorrhage not requiring surgical or endoscopic intervention (outpatient care).	Severe haemorrhage requiring inpatient care e.g. transfusion, surgical or endoscopic intervention.

haemorrhagic complications.

Majority of patients presented with features of thrombotic complications. Of these the main symptom was headache (figure 1) in 33 (23.2%) patients.

Forty four patients (31%) presented with bleeding tendencies, out of who twenty eight had grade I and eleven grade III bleeding.

Of the patients developing haematological complications there was significant association with the INR levels ($p = 0.017$). More women than men developed complications though not statistically significant ($p 0.38$). Of patients with haematologic complications 54% were educated to secondary level. Mean duration of anticoagulation for patients developing complications was 82.9 months (± 64 months), compared to 60.8 months (± 43.8 months) for those without.

Of 9 patients non-compliant with medications (not taking), 8 developed haematologic complications. No patient interrupting medication (compliant, but only interrupted from time to time) reported any complications (table 5).

Discussion

Control of INR remains a challenge in developing countries. Without adequate control haematologic complications are inevitable. This study recorded a complication rate of 54.9% and noncompliance rate of 9%, high by any standards. An association between poor compliance and occurrence of complications is in keeping with other studies. However, patients on short term interruption of medication were not associated with increased risk.

Bivariate analysis shows clinic visit interval as a weak association with development of complications ($p = 0.052$). As admitted by many patients, financial con-

straints make regular clinic attendance difficult. Coupled with this not all patients adhere to their medications as required making compliance and interruption of medication a major problem. We suspect some patients only commence warfarin a week before clinic due date giving INR results suggesting faithful compliance to medication. This behaviour is intended to maintain good doctor patient relationship .

The increased occurrence of complications is likely to be due therefore to a combination of noncompliance and associated to INR fluctuations. Previous studies here have shown a poor ability to maintain adequate anticoagulation with only a 6.9% of patients maintaining adequate control. Fluctuations of INR were associated with complications and our findings are consistent with similar results.

The duration of anticoagulation therapy is an independent predictor of haematologic complications. Longer duration of therapy positively associated with development of complications. A plausible explanation being that with risk of complication being present, the longer the duration the more likely a cumulative increase in the number of complications will occur. A local study showed that adequate anticoagulation was maintained for only 18% of follow up time⁸.

The level of patient education or socioeconomic status was not a risk factor for development of complications. This is in contrast to a South African study, which demonstrated a direct association with occurrence of haematologic complications. Generally education and age have a positive association with INR control. Increasing age has been shown to have a positive correlation with INR control. Having mixed patients of generally younger ages and education it is likely this relationship is lost in

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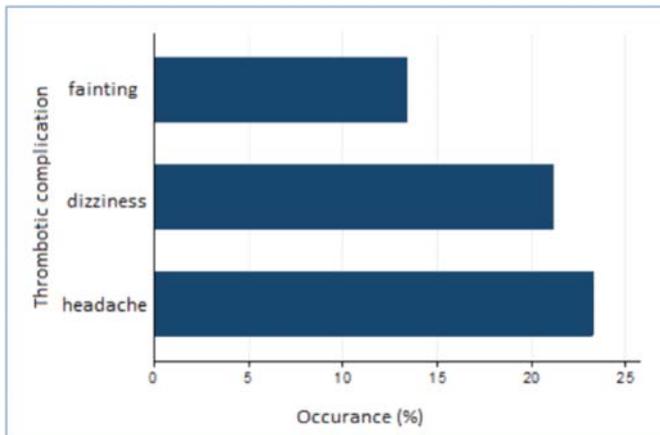


Figure 1. Thromboembolic complications

Variable	Value / %
Mean Age	29.61
Sex	
Male	55 (38.7)
Female	87 (61.3)
Highest Level of Education	
Primary	48 (33.8)
Secondary	62 (43.7)
Tertiary	21 (14.8)
Not documented	11 (7.7)
Occupation	
Formal	31 (21.8)
Informal	25 (17.6)
Student	30 (21.1)
Unemployed	51 (35.9)
Not documented	5 (3.5)

Table 2: Demographic Characteristics

our analysis.

The type of surgery performed was not a risk factor for the occurrence of complications, 54.7% of patients with complications having undergone mitral valve replacement surgery. However, this could be attributed to mitral valve replacement being the most common surgery. A South African study showed a higher incidence of haematologic complications in patients who had undergone double valve replacement than in patients who had single valve surgery.

Conclusions

Our valve patients on warfarin follow up experience a high complication rate that will need to be addressed. Development of complications is associated INR con-

Variable	Frequency/ (%)
Type of surgery	
Mitral valve replacement	73 (51.4)
Aortic valve replacement	35 (24.6)
Double valve replacement	34 (23.9)
Intervals between clinic visits (months)	
< 3 months	80 (56.33)
4 – 6 months	56 (39.43)
7 – 12 months	5 (3.52)
Compliance to medication (n=39)	
Yes	30
No	9
Interruption of anticoagulation (n=39)	
Yes	4
No	35
Presence of bleeding tendencies (n=142)	
Yes	44 (31)
No	71 (50)
Not documented	27 (19)
Grade of bleeding tendency	
I	28 (63.6)
II	11 (25.0)
III	4 (9.1)
Missing data	1 (2.3)
Thromboembolic incidents	
Dizziness	
Yes	30
No	84
Fainting	
Yes	19
No	95
Headaches	
Yes	33
No	81

Table 3: Clinical Characteristics

trol, compliance to medication, interruption of medication and duration of anticoagulation. Of all these variables only duration of anticoagulation is an independent predictor of haematologic complications.

Recommendations

Identified risk factors can be remedied by ensuring patients are fully educated on the gravity of complications associated with non-compliance. One option would be stricter patient follow up. However, this places great financial burden on the patients, most of who have to travel very long distances for follow up. Estimations of INR are only possible in Nairobi. For this reason self-management of anticoagulation practiced in the West may not be a solution for us either .

Viable alternative would be the establishment of other laboratories outside Nairobi where patients can have their INR monitored. Establishment of other cardiotho-

Variable	Haematologic complications		p value
	Yes (freq/ %)	No (freq/ %)	
Sex			0.308
Male	23 (34.3)	32 (42.7)	
Female	44 (65.7)	43 (57.3)	
Highest Level of Education			0.186
Primary	22 (32.8)	26 (34.7)	
Secondary	32 (47.8)	30 (40.0)	
Tertiary	11 (16.4)	10 (13.3)	
Occupation			0.688
Formal	16 (23.9)	15 (20.0)	
Informal	13 (19.4)	12 (16.0)	
Duration of anticoagulation (months) (Mean /SD)	82.9 (64.0)	60.8 (43.8)	0.001
Type of surgery			0.668
Mitral valve replacement	41 (54.7)	32 (47.8)	
Aortic valve replacement	18 (24.0)	17 (25.4)	
Double valve replacement	16 (21.3)	18 (26.9)	
Intervals between clinic visits (months)			0.052
1	33 (23.23)	16 (11.26)	
2	19 (13.38)	21 (14.78)	
3	11 (7.74)	19 (13.38)	
4	12 (8.45)	10 (7.04)	
>4	0 (0)	1 (0.7)	
Number of clinic visits/year			0.344
0	1 (2.3)	0	
1	6 (13.6)	15 (21.4)	
2	5 (11.4)	10 (14.3)	
3	7 (15.9)	9 (12.9)	
4	13 (29.5)	26 (37.1)	
5	3 (6.8)	0	
6	7 (15.9)	7 (10)	
7	1 (2.3)	1 (1.4)	
12	1 (2.3)	2 (2.9)	
Compliance to medication			0.040
Yes	14	16	
No	8	1	
Interruption of anticoagulation			0.041
Yes	0	4	
No	20	15	

Table 4: Associations between predetermined risk factors and haematologic complications

Label	Estimate	Confidence interval	p value
Age centred	0.99	0.95,1.02	0.471
Male vs female	0.84	0.33,2.09	0.703
Advanced vs basic education	0.82	0.32,2.12	0.682
Visits:3-4 vs <3	0.47	0.10,2.09	0.319
5-6 vs <3	1.15	0.12,10.86	0.901
7-12 vs <3	0.41	0.04,4.10	0.445
Duration of anticoagulation	14.99	3.90,218.70	0.005
INR levels	1.58	0.75,3.33	0.229

Table 5: Multivariate regression analysis for occurrence of haematologic complications

racic centres distributed throughout the country would be the eventual solution.

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