Title

Comparison of Warfarin versus Rivaroxaban in management of post myocardial infarction left ventricular thrombus in a tertiary cardiac centre of Nepal: a Randomized control study.

Submitted to
National Health Research Council
Kathmandu, Nepal

Submitted by
Dr. Dipanker Prajapati
18th November 2024

Study team: Dr Dipanker Prajapati, Dr Chandra Mani Adhikari, Dr. Rolina Dhital, Suraksha Dhungana, Sujata Sapkota, Dr. Reeju Manandhar, Dr. Binay Kumar Rauniyar, Dr. Birat Krishna Timalsena, Dr. Rikesh Tamrakar, Dr. Parash Koirala, Dr. Nirmal Prasad Neupane, Dr. Murari Dhungana, Indesh Thakur

Date: 18th November 2024 (3rd Mangsir 2081)

To,
The Member-Secretary (Executive Chief)
NHRC

Subject: Submission of Final Research Report of Provincial Health Research Grant

Dear Sir,

I am a Principal Investigator of the Provincial Health Research Grant FY 2079/080 offered by Nepal Health Research Council (NHRC) for the study titled "Comparison of Warfarin versus Rivaroxaban in management of post-myocardial infarction left ventricular thrombus in a tertiary cardiac center of Nepal: a Randomized control study" on 16th March 2023. As per the Contractual Service Agreement (received on 2nd June 2023), I have been asked to submit the final research report by June 2024.

I am attaching the final report of the study of last year. Due to low enrollment, the conduction of the study is being delayed at present.

Looking forward to receiving a kind response.

Thanking you once again,

Sincerely yours,

Name : Dr. Dipanker Prajapati
Affiliation : Consultant Cardiologist,
Head of Department,
Department of Cardiology,
Shahid Gangalal National Heart Centre
Phone No : 01-6612701, 9849273202
Email : dpcardio@hotmail.com

Government of Nepal

Nepal Health Research Council (NHRC)

Estd. 1991

Ref. No.: 2272

16th March 2023

Dr. Dipanker Prajapati

Shahid Gangalal National Heart Center

Kathamndu, Nepal

Subject: Approval letter for Grant

Dear Dr. Dipanker Prajapati,

We would like to express our congratulations on the approval of the Provincial Health Research Grant FY 2079/080 offered by Nepal Health Research Council (NHRC). Our approved amount is Nrs 5,00,000 for the purpose of your research **"Comparison of Warfarin versus Rivaroxaban in management of post-myocardial infarction left ventricular thrombus in a tertiary cardiac center of Nepal: a Randomized control study".** Please proceed further with the ethical approval process.

We hope that your research is a success and results in benefitting the entire society.

If any further discussion is needed in regard to this matter, please do not hesitate to contact Capacity Building Section.

.....

Dr. Pradeep Gyanwali

Member-Secretory (Executive Chief)

NHRC

Contractual Service Agreement

(CSA)

An agreement made between the Nepal Health Research Council and the Contractor on 20th February, 2023

Dr. Dipanker Prajapati Principal Investigator (hereafter, Contractor) has been awarded by Nepal Health Research Council (NHRC) for the **Provincial Health Research Grant** of the Fiscal Year 2079/2080 entitled " **Comparison of Warfarin versus Rivaroxaban in management of post-myocardial infarction left ventricular thrombus in a tertiary cardiac center of Nepal: a Randomized control study** " on the terms and conditions mentioned below:

1. **Nature of the service:** The contractor should initiate the research work after the agreement with NHRC and submit final research report latest by June 13, 2023 (30th Jestha 2080).

2. **Duration of the project:** The duration of the study is six months.

3. **Payment schedule:**

   After signing the agreement -50%
   After Submission of Final Report -50%
   The Total amount: Nrs 500000

4. **Deliverables:**
   - Submit two copies of the final report in hard binding copy.
   - Provide the electronic version of the final report.

5. **Income tax:**
   NHRC will deduct tax as per rule of Government of Nepal.

6. In cases where the contractor does not submit the completed project reports within the timeline agreed between the parties, the contractor is obliged to return the whole amount provided by the NHRC. If the solution is not found, NHRC reserves the right to take legal action according to applicable laws of the government of Nepal.

.....
Dr Pradip Gyanwali
Member-Secretory (Executive Chief)
NHRC

.....
Dr. Dipanker Prajapati
Principal Investigator

Government of Nepal

Nepal Health Research Council (NHRC)

Estd. 1991

Ref. No.: 3578

18 June 2023

Dr. Dipanker Prajapati

Principal Investigator

Shahid Gangalal National Heart Centre (SGNHC)

Kathmandu

Ref: Approval of research proposal

Dear Dr. Prajapati,

This is to certify that the following protocol and related documents have been granted approval by the Ethical Review Board, NHRC for implementation.

If the researcher requires transfer of the bio-samples to other countries, the investigator should apply to the NHRC for the permission. The researchers will not be allowed to ship any raw/crude human biomaterial outside the country, only extracted and amplified samples can be taken to laboratories outside of Nepal for specific study, as per the protocol submitted and approved by the NHRC. The remaining samples of the lab should be destroyed as per standard operating procedure and the process should be documented and informed to the NHRC timely.

ERB Protocol No/ Submitted Date	166/2023 10 March 2023	**Sponsor Protocol No**	NA
Principal Investigator's	Dr. Dipanker Prajapati	**Sponsor Institution**	NHRC Grant
Title	Comparison of Warfarin versus Rivaroxaban in management of post myocardial infarction left ventricular thrombus in a tertiary cardiac centre of Nepal: a Randomized control study		
Protocol Version No	NA	**Version Date**	NA
ICF Version No. (V.N.)	NA	**Version Date**	NA
Other Documents 1. Data collection tools 2. GCP certificated 3. Commitment letter for Management of SAE 4. Role and responsibilities 5. Conflict of Interest of DSMB Board 6. IRC Support letter 7. Detailed Investigators brochure 8. SAE Management plan 9. Standard Operating Procedure 10. Work plan			
Co-Investigator's	1. Chandra Mani Adhikari 2. Rolina Dhital 3. Suraksha Dhungana		

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Ref. No.: 3578

	4. Sujata Sapkota 5. Reeju Manandhar 6. Binay Kumar Rauniyar 7. Birat Krishna Timalsena 8. Rikesh Tamrakar 9. Parash Koirala 10. Nirmal Prasad Neupane 11. Murari Dhungana 12. Indesh Thakur			
Study Site	Shahid Gangalal National Heart Centre (SGNHC), Kathmandu			
Type of Review	☐	Expedited	**Timeline of Study** September 2022 to June 2024 **Duration of Approval** 18 June 2023 to June 2024 **This approval will be valid only one year**	**Frequency of continuing review** NA
	√	**Full Board**		
	Meeting Date: 7 June 2023			
Total budget of research	**NRs 500,000.00**			
Ethical review processing fee	**Waived as the researcher had received NHRC Grant fiscal year 2079/2080**			

Investigator Responsibilities

- If you do not start the project within 3 months of this letter, please contact the Ethical Review M & E Section at NHRC
- Submit and get approval for any changes in approved protocol before its implementation
- Submit Serious Adverse Events (SAE) and Suspected Unexpected Serious Adverse Reaction (SUSAR) reports to the ERB within 2 weeks of the investigator becoming aware of the event
- Submit progress report every 6 months
- Submit the site close out report after completion of protocol procedures at the study site and final report within 3 months of study completion.
- Report major protocol deviation / violation within 7 days
- Comply with all relevant international and national guidelines
- Abide by the principles of Good Clinical Practice and ethical conduct of the research

If you have any questions, please contact the Ethical Review M & E Section at NHRC.

Thanking you,

.....

Dr. Pradip Gyanwali
Member Secretary

Tel: +977 1 4254220, Ramshah Path, PO Box: 7626, Kathmandu, Nepal
Website: http://www.nhrc.gov.np, E-mail: nhrc@nhrc.gov.np

Declaration

I, Dipanker Prajapati, the Principal Investigator of this research, on behalf of all team members, declare that this research study, titled "Comparison of Warfarin versus Rivaroxaban in management of post myocardial infarction left ventricular thrombus in a tertiary cardiac centre of Nepal: a Randomized control study." is our original work. All data and information source used in this study has been duly acknowledged through proper citation.

We also declare that the research has been conducted with highest ethical standards; and, all activities have been carried out in accordance with the guidelines and regulations of the Nepal Health Research Council Ethical Board. Informed consent was obtained from all participants and their confidentiality maintained.

We have duly acknowledged the all supporters, contributions and funders of this research.

Date: November 15 2024

Name **: Dr. Dipanker Prajapati**

Affiliation **: Consultant Cardiologist,**

Head of Department,

Department of Cardiology,

Shahid Gangalal National Heart Centre

Phone No **: 01-6612701, 9849273202**

Email **: dpcardio@hotmail.com**

Conflicts of Interest declaration form

Research title: Comparison of Warfarin versus Rivaroxaban in management of post-myocardial infarction left ventricular thrombus in a tertiary cardiac center of Nepal: A Randomized control study.

The **Researchers** whose names are listed immediately below certify that they have **no affiliations** with or **involvement in any organization** or **entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership,** or **other equity interest; and expert testimony or patent-licensing arrangements),** or **non-financial interest (such as personal** or **professional relationships, affiliations, knowledge or beliefs) in the subject matter** or **materials discussed in this research proposal.** The researchers whose names are listed below submit this disclosure of conflict of interest to the Ethical Review Board (ERB of Nepal Health Research Council (NHRC) to allow a fair review to be conducted.

I/we report the following details of **affiliation** or **involvement in an organization** or **entity with a financial** or **non-financial interest in the subject matter** or **materials discussed in this research proposal.** Please specify the nature of the conflict on a separate sheet of paper if the space below is inadequate.

Researcher's names:

We hereby sign these statements to indicate agreement that the above information is true and correct (*a photocopy of this form may be used if there are more than 10 researchers*):

Researcher's name (typed)	Affiliation	Researcher's signature	Date
Dr. Dipanker Prajapati	Shahid Gangalal National Heart Centre (SGNHC)		29th March 2023
Dr. Chandra Mani Adhikari	SGNHC		29th March 2023
Dr. Rolina Dhital	Health Action and Research		29th March 2023
Mrs. Suraksha Dhungana	SGNHC		29th March 2023
Dr. Sujata Sapkota	Manmohan Memorial Institute of Health Sciences		29th March 2023
Dr. Binay Kumar Rauniyar	SGNHC		29th March 2023
Dr. Birat Krishna Timalsena	SGNHC		29th March 2023
Dr. Rikesh Tamrakar	SGNHC		29th March 2023
Dr. Parash Koirala	SGNHC		29th March 2023
Dr. Nirmal Prasad Neupane	SGNHC		29th March 2023
Dr. Murari Dhungana	SGNHC		29th March 2023
Mr. Indesh Thakur	SGNHC		29th March 2023
DR REESU MANANDHAR	SGNHC		29th March 2023

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Chapter 1 Introduction

1.1 Background

Cardiovascular disease is the leading cause of mortality and morbidity among non-communicable diseases worldwide including in Nepal. Myocardial infarction (MI) is the main disease among cardiovascular diseases. [i] MI is also the main reason for hospitalization in the cardiac centers of our country. [ii] There is an additional burden of late presentation of MI in our setting due to lack of proper awareness, limited access to health care and improper referral mechanism. In the hospital-based registry 2018, more than 65% of acute MI presented after the eligible time frame for primary angioplasty or thrombolysis. [iii]

The incidence of left ventricular (LV) thrombus formation is increased with the late presentation. Worldwide, the prevalence of LV thrombus before the era of primary angioplasty was around 31-57%. [iv], [v], [vi] After the start of the primary angioplasty techniques, the prevalence of post-MI LV thrombus has decreased to around 15%. [vii] However, it is still associated with increased embolic events and mortality risks. [viii], [ix],[x]

European and American guidelines have recommended using vitamin K antagonist (VKA) for a minimum of 3-6 months as a class IIa, LOE c, with duration individualized to bleeding risk with a target of international normalized ratio (INR) of 2.5 (range of 2 to 3). [xi],[xii] Non-VKA oral anticoagulants (NOACs) in addition to the dual antiplatelet therapy in these patients are attractive alternatives because of their potential efficacy and safety along with ease of administration, lack of requirement for INR monitoring or dietary restrictions resulting in overall improvement of life.[xiii] Warfarin and NOACs including Rivaroxaban both have been used for post-myocardial infarction left ventricular thrombus, which is also evident in different observational studies.[xv] However, there is no randomized control trial comparing warfarin and NOACs. There are two ongoing trials NCT01556659 and NCT03764241. The recommendation is more relevant to us as we are overburdened with late presenters due to various reasons. This study was designed for the evaluation of anticoagulation effects among the acute ST elevation Myocardial Infarction (STEMI) with LV thrombus in complete resolution of LV thrombus. We aim to compare Warfarin to Rivaroxaban in the management of post-myocardial infarction left ventricular thrombus in our part of the world.

1.2 Conceptual framework of the study

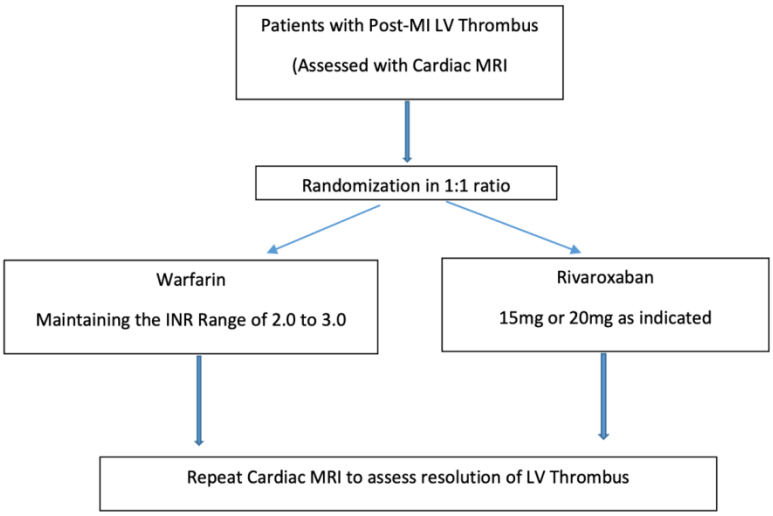


Fig. Study framework

1.3 Statement of the problem

This study is a first of its kind being conducted in Nepal. There is no randomized controlled study of STEMI patients focusing on the management of LV thrombus done to date in Nepal. This study is thought to provide significant national data for the change in the management of late presentation MI in Nepal. The outcome will help manage the STEMI patients among whom large numbers present late to tertiary centers. The proposed study will generate the much-needed data for such patients who are treated with either warfarin (with or without INR monitoring) or only with dual antiplatelet without the use of anticoagulation till now. The use of dual antiplatelet agents without anticoagulation might significantly affect the management of MI as we lack data on such individuals.

The proposed study will establish the importance of anticoagulation among post-MI LV thrombus patients. We can generate data that will be helpful in the international community for further multicenter research. As the post-MI LV thrombus is common in our part of the world due to delayed presentation, we feel the generation of such data is much more important to countries facing a similar obstacle in the management of STEMI. Moreover, proper conduct of such RCT in our institution will help in increasing our capacity building to conduct RCT in the future. Furthermore, this study will show how such research is feasible in low to middle-income countries like Nepal and can change our research capabilities of ours.

1.4 Objectives of the study

General Objective:

To compare Warfarin and Rivaroxaban in the complete resolution of LV thrombus in patients with post-myocardial infarction left ventricular thrombus in a tertiary cardiac center in Nepal.

Specific Objective:

1) To assess the differences in the effect of Warfarin and Rivaroxaban in the management of post-myocardial infarction left ventricular thrombus
We measured the effect in terms of complete resolution of left ventricular thrombus assessed by cardiac MRI 3 months after the treatment.

2) To assess the difference in the incidence of major bleeding in patients after the treatment between warfarin or rivaroxaban in post-myocardial patients with LV thrombus.

We assessed the bleeding events as defined by the International Society on Thrombosis and Haemostasis (ISTH)/Scientific and Standardization Committee (SSC) for non-surgical patients and includes a clinically relevant minor bleed (an acute or subacute clinically overt bleed that does not meet the criteria for a major bleed but prompts a clinical response, in that it leads to at least one of the following 1. Hospital admission for bleeding, or 2. A physician-guided medical or surgical treatment for bleeding, or 3. A change in antithrombotic therapy (including interruption or discontinuation of study drug).) and major bleeding which included 1. Fatal bleeding. and/or 2. Symptomatic bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, retroperitoneal, intraarticular or pericardial, or intramuscular with compartment syndrome. and/or 3. Bleeding causing a fall in hemoglobin level of 2 g/dL (1.24 mmol/L) or more, or leading to transfusion of two or more units of whole blood or red cells.

3) To assess the difference in the incidence of embolic events in patients after the treatment between warfarin or rivaroxaban in post-myocardial patients with LV thrombus.

We assessed Embolic events as defined by the Guideline for the Prevention of Stroke in Patients with Stroke and Transient Ischemic Attack Cardioembolic stroke which includes stroke attributable to arterial occlusion from an embolus that presumably arose in the heart. Ischemic stroke in the vascular distribution of a major intracranial or extracranial artery with >50% stenosis or occlusion on vascular imaging.

Chapter 2 Methodology

2.1 Study method and design

The study incorporated the randomized controlled trial design with a parallel group and 1:1 allocation ratio for this research. Single masking of the outcome assessor was employed.

2.2 Study area

Shahid Gangalal national heart centre (SGNHC) is a tertiary cardiac care center in Nepal providing its services to cardiac patients from all over Nepal since 1995 and an average of 11,000 patients are admitted every year. SGNHC is one of the leading hospitals in Nepal and the best among those that specialize in cardiac care. STEMI is the most common cause of mortality and admission in coronary care units and wards in the tertiary cardiac center of Nepal. The majority of the patients present late to the hospital after the symptom onset and were not candidates for primary coronary intervention. The type of care provided to the STEMI patients in this hospital directly reflects the standard of care of STEMI of the entire nation as a huge proportion of STEMI patients are being treated here and in other hospitals and the practitioner considers the treatment protocol of this center as a national standard. In addition, significant numbers of cardiologists from Nepal are trained here and will follow the same pattern of treatment and practice similarly while working in various hospitals in Nepal. Therefore, management of the STEMI patients with LV thrombus will contribute significantly to making a positive change in the management of post-MI throughout the nation.

2.3 Study population

The study population was all adult patients aged more than 18 years and the cardiac MRI diagnosed left ventricular thrombus in patients who had a recent myocardial infarction. The duration of the acute event varied among our study population. All the patients who were diagnosed as a case of LV thrombus were included in our study. The patients were contacted after getting information from the cardiac MRI laboratory of the center. The patients were informed about our research and were included only after obtaining written consent.

The recent meta-analysis which included one randomized clinical trial and 5 retrospective observational studies has shown a thrombus resolution of 79% in the Rivaroxaban group and 60% in the Warfarin group. With the 95% confidence interval and 80% power, the sample size calculation was performed using the formula comparing the two proportions. The sample size calculated was 89 in each group. With the 10% non-response rate, the final sample size was determined to be 98 in each group. (Saleh Y, Al-Abcha A, Abdelkarim O, Elwany M, Abdelfattah OM, Abdelnabi M, Almaghraby A. Meta-Analysis Comparing the Effect of Rivaroxaban Versus Vitamin K Antagonists for

Treatment of Left Ventricular Thrombi. Am J Cardiol. 2021 Dec 15;161:123-125. doi: 10.1016/j.amjcard.2021.09.009. Epub 2021 Oct 14. PMID: 34656296.)

2.4 Sampling Technique

Open-label 1:1 ratio randomized sampling method was used for the study. The patients who fit into the eligibility criteria and provided informed consent were enrolled in the study. The patients were provided with study ID numbers. The patients enrolled in the study were randomized in a 1:1 ratio into either of the two groups. The randomization of the patients was done through computer-generated random numbers for either of the groups. A research officer from SGNHC, independent of the intervention, was responsible for randomization. The allocation to either of the groups was concealed at the time of the randomization. The randomization of the patients to either of the groups was completed when the required sample size was met for each group. When a patient with an assigned random number refused to participate in the study after the randomization, another random number was generated for the randomization of another patient. Since the patients who were treated with Warfarin need frequent INR monitoring with blood investigation, the patient and the treating physician along with the research officer were not blinded in our research. However, the assessors of the LV thrombus that is the radiologists and the radiographers along with the statistician and coinvestigators who were responsible for the data analysis were blinded to the randomization process. The allocation concealment was performed by the principal investigator and the research officer.

2.5 Data Collection Tools and Techniques

Data Collection Technique

Recruitment: We contacted all the patients admitted with the inclusion criteria in the center. The details of the study were explained along with the randomization process. The participants were included in the study only when they provided written consent. The recruitment process started only after approval by the Nepal Health Research Council.

Baseline data collection: The research officer was trained for the baseline data collection. Once the LV thrombus was diagnosed in the Cardiac MRI laboratory, the research officer was informed. The research officer then contacted the patient and their family and started the recruitment process.

Follow-up data collection: Follow-up data was also collected by the research officer. The patients were contacted before the end of the three-month follow-up. They were requested for a repeat cardiac MRI and the result of the cardiac MRI was followed by the research officer.

Data collection tools

A case report form (CRF) was designed to record all protocol-required information on each subject in our clinical research study. The CRF included 5 sections which included the following parameters. The first section consisted of demographic and

clinical parameters like age, sex, cardiovascular risk factors (Smoking, diabetes mellitus, physical inactivity, BMI, dyslipidemia, blood pressure, etc), type of myocardial infarction, and timing of an acute event. The second section consisted of echocardiographic parameters which included LV Ejection Fraction, LV wall motion, involvement of LV apex, diastolic dysfunction, infarct size, LV thrombus size and its mobility. The third section consisted of Cardiac MRI parameters which included LV Ejection Fraction, LV wall motion, involvement of LV apex, infarct size, LV thrombus size and its mobility, The fourth section consisted of the embolic and bleeding events which included both the major bleeding events and clinically relevant minor bleeding events. The fifth section consisted of the follow-up cardiac MRI findings which included the presence or absence of LV thrombus and the size and mobility of the thrombus if the thrombus was present.

2.6 Validity of the instruments

The case report forms, consent forms and patient information forms were constructed after consultation with different experts from different departments of the center.

2.7 Data collection procedure

Our study employed a randomized controlled trial. The patients who were diagnosed with a case of post-myocardial infarction LV thrombus in the Cardiac MRI laboratory were contacted by our research officer. Details of the research and need for anticoagulation, its benefits and risks and possible embolic phenomenon if not treated and possible bleeding tendency during the treatment with anticoagulation were explained. We included the patients in the study once the informed consent was signed.

Randomization: The patients were randomly allocated to the Warfarin group and the Rivaroxaban group. The randomization was based on a single sequence of random assignments which were carried out with the computer-generated random numbers using the Microsoft Excel version 2016 using the function RAND (). An independent researcher made random allocation cards using computer-generated random numbers for both the control and intervention groups. The original random allocation sequences were stored in an inaccessible third place and the researcher worked with a copy. Allocated random sequences were printed separately and sealed in an envelope for each one and put in an envelope after being folded several times. The inside of the envelope was not visible from the outside. There were serial numbers on the outside of the envelopes. The research assistant used the envelope serially for each included patient. Recruited date, time, patient ID, and allocated sequence number were recorded on a separate register.

Control (Warfarin) Group: The patients in the control group were treated with Warfarin FARIN from Quest Pharmaceuticals Private Limited in Nepal. The baseline PT/INR was assessed before starting the drug. The dose was started with 5 mg and was titrated based on the International Normalized Ratio (INR) which was targeted at the range of 2.0 to 3.0. The dual antiplatelet duration was based on the latest guidelines. The

patients were asked for frequent INR monitoring on an OPD basis until the INR was within the therapeutic range, after which patients were asked for monthly follow-ups with the INR reports. The patients in the control group were not treated with heparin or low molecular weight heparin before the INR was maintained in the therapeutic range.

Intervention (Rivaroxaban) Group: The patients in the intervention group were treated with Rivaroxaban 20 mg (RIVOXAN from National Healthcare Private Limited) once daily with the evening meal in patients with a CrCl >50 mL/min OR 15 mg in cases of moderate-to-severe renal impairment dose with the dosing of once daily with the evening meal in patients with a CrCl ≤50 mL/min. The patients in the intervention group were requested for follow-up after 3 months of commencing the treatment or whenever the signs and symptoms of bleeding events were noted. At the end of the 3 months of the treatment, the patients underwent repeat cardiac MRI for evaluation of the presence or absence of the LV thrombus.

Blinding: Due to the different modes of administration and monitoring of the patients in the intervention group, the blinding of the researcher, research assistant and patient was impossible in our study. However, the assessors, who are radiographers and radiologists, responsible for assessing the primary outcome of the study which is the resolution of the left ventricular thrombus, were blinded to the control and intervention group.

Follow-up procedures: The follow-up procedures were different for the two groups as the administration and monitoring modes were different for the two groups. In the control group, patients were required frequently to check the PT/INR and report to the research assistant, the research assistant titrated the dose of the warfarin as per the INR report of the patient. This required frequent follow-up (once or twice weekly). Once the INR was within the range of 2.0 to 3.0, the frequency of INR monitoring was decreased according to the need (Once or twice a month). Follow-up lasted till 3 months after the start of the treatment after which the outcome assessment was performed with a Cardiac MRI. In the intervention group, patients were requested for follow-up if they developed any clinical symptoms of embolic or bleeding events. If not, all patients were followed up after 3 months of treatment and then the primary outcome was assessed by Cardiac MRI.

2.8 Data processing

Data were collected and entered in the computer-based CRF constructed using the password-protected free software at https://www.kobotoolbox.org. The data was accessed by the principal investigator and the research officer only. The names of the participants were anonymized using the initials only. The data were downloaded in the Excel version and transferred to SPSS for statistical analysis. The data were anonymized before statistical analysis which was performed by the separate coinvestigators who were responsible for the data analysis.

2.9 Data analysis

The Statistical analysis was conducted based on intention-to-treat analysis. Continuous data is presented as the mean ± standard deviation or the median with an interquartile range. Categorical data is presented as counts and percentages. The rate of LVT resolution is compared using the Chi-square test. Time to LVT resolution and adverse events are expressed by Kaplan-Meier curves and compared by the log-rank test. All P values are two-sided, and the statistical significance is set at a 5% level. The proportion and 95% confidence interval (CI) are calculated. A 'P' value of less than 0.05 is considered significant.

2.10 Delimitations of the study

This study has a limitation in that it is a single-center study.

2.11 Ethical considerations

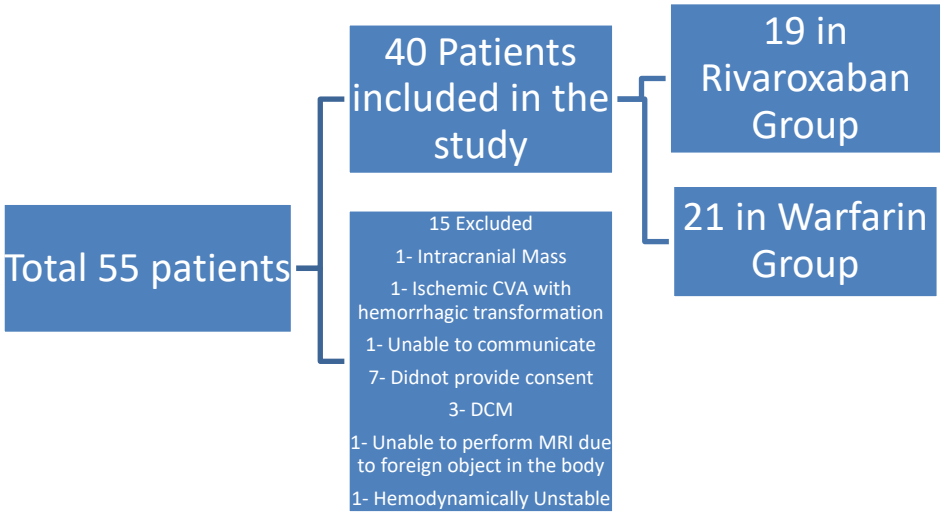
Our study proposal has been registered in ClinicalTrials.gov (NCT05794399). The study was also approved by the Nepal Health Research Council before its commencement. (ERB Protocol No:166/2023)

The patients were informed about our research and were included only after obtaining written consent.

Chapter 3 Data Analysis

3.1 Uni-variate findings of socio-demographic and other variables/characteristics

	Warfarin Group	Rivoroxaban Group
Characteristics	**21**	**19**
Age (Mean) in years	59.21±14.2	54.58±14.2
Male	17	16
Female	4	3



3.2 Bivariate and other statistical findings for each hypothesis/research question

	Warfarin Group (n=21)	**Rivaroxaban Group (n=19)**
Resolution of Thrombus	7 (33.4%)	9 (47.4%)
No Resolution of Thrombus	8 (38.1%)	4 (21.1%)
Follow up remaining	5	1
Loss to follow up	1 (4.7%)	1 (5.3%)
Death due to Cardiovascular causes	3 (14.3%)	0
CVA	1(4.7%)	0

3.3 Interpretation/discussion on findings

Among the 40 patients who were recruited, 27 have completed the follow-up. During the analysis, the resolution of LV thrombus was more common in the Rivaroxaban group compared to the Warfarin group. However, these are preliminary results and the absolute comparison can only be performed after full recruitment.

3.4 Conclusion

In this preliminary analysis, the resolution of LV thrombus is higher in the rivaroxaban group than in the Warfarin group.

3.5 Dissemination plan

We plan to publish the finding in indexed journal and present in the national and international conferences. We also plan to inform the findings to the important stakeholders of the health.

References

[i] Bhattarai S, Aryal A, Pyakurel M, Bajracharya S, Baral P, Citrin D, Cox H, Dhimal M, Fitzpatrick A, Jha AK, Jha N, Karmacharya BM, Koju R, Maharjan R, Oli N, Pyakurel P, Sapkota BP, Shrestha R, Shrestha S, Spiegelman D, Vaidya A, Shrestha A. Cardiovascular disease trends in Nepal - An analysis of global burden of disease data 2017. Int J Cardiol Heart Vasc. 2020 Jul 31;30:100602. doi: 10.1016/j.ijcha.2020.100602. PMID: 32775605; PMCID: PMC7399110.

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DATA COLLECTION TOOL

Section 1: Demographic and Clinical Parameters

Name		Sex		Age (in years)	
Weight (in Kg		Height in cm			
Smoking	Yes Quit: No Since	Physical Activity (hours per week)		Diabetes Mellitus	
HTN	Yes on medication: No				
Dyslipidemia	Yes on medication: No				
Tobacco:	Yes Quit: No Since				
Type of Myocardial infarction		Timing of chest pain (in hours) before presentation to Emergency and thrombolysis/PCI			
Antiplatelets taking at present	Aspirin: Duration: Clopidogrel: Duration: Ticaglelor: Duration:	Prasugrel: Duration:			

Section 2: Echocardiographic Parameters

LV Ejection Fraction:		Diastolic Dysfunction:	
LV Wall Motion Abnormality:			
	Base	Mid	Apical
Anterior Wall			
Anteroseptal Wall			
Inferoseptal Wall (Septal)			
Inferior Wall			
Anterolateral (Lateral) Wall			
Inferolateral (Posterior) wall			
LV Apex			
LV Thrombus		LV Thrombus Mobility	

Section 3: Cardiac MRI Findings

LV Ejection Fraction:			
LV Wall Motion Abnormality:			
	Base	Mid	Apical
Anterior Wall			
Anteroseptal Wall			
Inferoseptal Wall (Septal)			
Inferior Wall			
Anterolateral (Lateral) Wall			
Inferolateral (Posterior) wall			
LV Apex			
LV Thrombus		LV Thrombus Mobility	

Section 4: Bleeding and Embolic Events

Bleeding events		Embolic Events	TIA: CVA: Territory:
Clinically relevant minor bleeding events:			
Treatment provided			

Section 5: Follow-up cardiac MRI findings

LV Thrombus	Present Absent	Size if present	Mobility if present

Comparison of Warfarin versus Rivaroxaban in management of post-myocardial infarction left ventricular thrombus in a tertiary cardiac center of Nepal: A Randomized control study."

Patient safety and adverse events

Warfarin

- Common ADR (1in10 users): periods that are heavier and last longer than usual, bleeding for a little longer than usual if you cut yourself, occasional nosebleeds (that last for less than 10 minutes), bleeding from your gums when you brush your teeth, ruises that come up more easily and take longer to fade than usual.
- Uncommon ADR (1to10 in 1000 users): Tiredness and lack of energy, shortness of breth, feeling dizzy or light-headed, a mild rash.
- Not known (frequency cannot be estimated from the available data): malaise with hypotension, blood clots, convulsions, vision disturbances, allergic reactions

Serious Adverse Events (SAE): An AE is considered serious if it poses a threat to the patient's life or functioning (E.g., death or at risk of death). For Rivaroxaban and Warfarin, it is

1. Serious bleeding, occasionally, this can be dangerous and needs urgent medical attention.
2. Bleeding in the brain. Very rarely, bleeding in the brain can occur.

Unexpected adverse event: For marketed drugs, unexpected adverse event is defined as (by FDA)

- An AE that is not listed in the drug's current labeling, or
- An AE that is more severe or more specific than indicated in the labeling.

Assessing an Adverse Event

The protocol has specified the duration that information on AEs will be collected. All AEs that occur in any clinical study participant will be assessed for:

- Severity

Serious AE different from severe AE. Serious refers to AE that poses risk to life or functioning. Severe refers to intensity of specific events (e.g., mild, moderate or severe pain). Severity and seriousness will be assessed by treating physician.

- Relatedness

AE may or may not related to the study interventions. This will be judged by the treating physician. Data managers who have no role in patient's management has no role in the judgement of severity and relatedness of the AE.
Initial reports of the adverse events could be reported by patients, nurses, family members or on duty doctors. These events will be documented in the patient's source documents including patients progress notes. Investigator team will verify the adverse events.

Adverse Event Reporting

All the severe and serious adverse events will be first reported to the principal investigator. The principal investigator will then report it to the SGNHC research unit and SGNHC IRB.

Adverse Event Follow-Up
All SAEs should be followed until resolution, or until the condition has stabilized with no further change expected.

Data safety management board (DSMB)

1. Dr Sujeeb Rajbhandari
Head of Deaprtment
Department of Cardiology
Chairman, Institutional Review Committee
Shahid Gangalal National Heart Center
sujeebr@hotmail.com, 9851066122

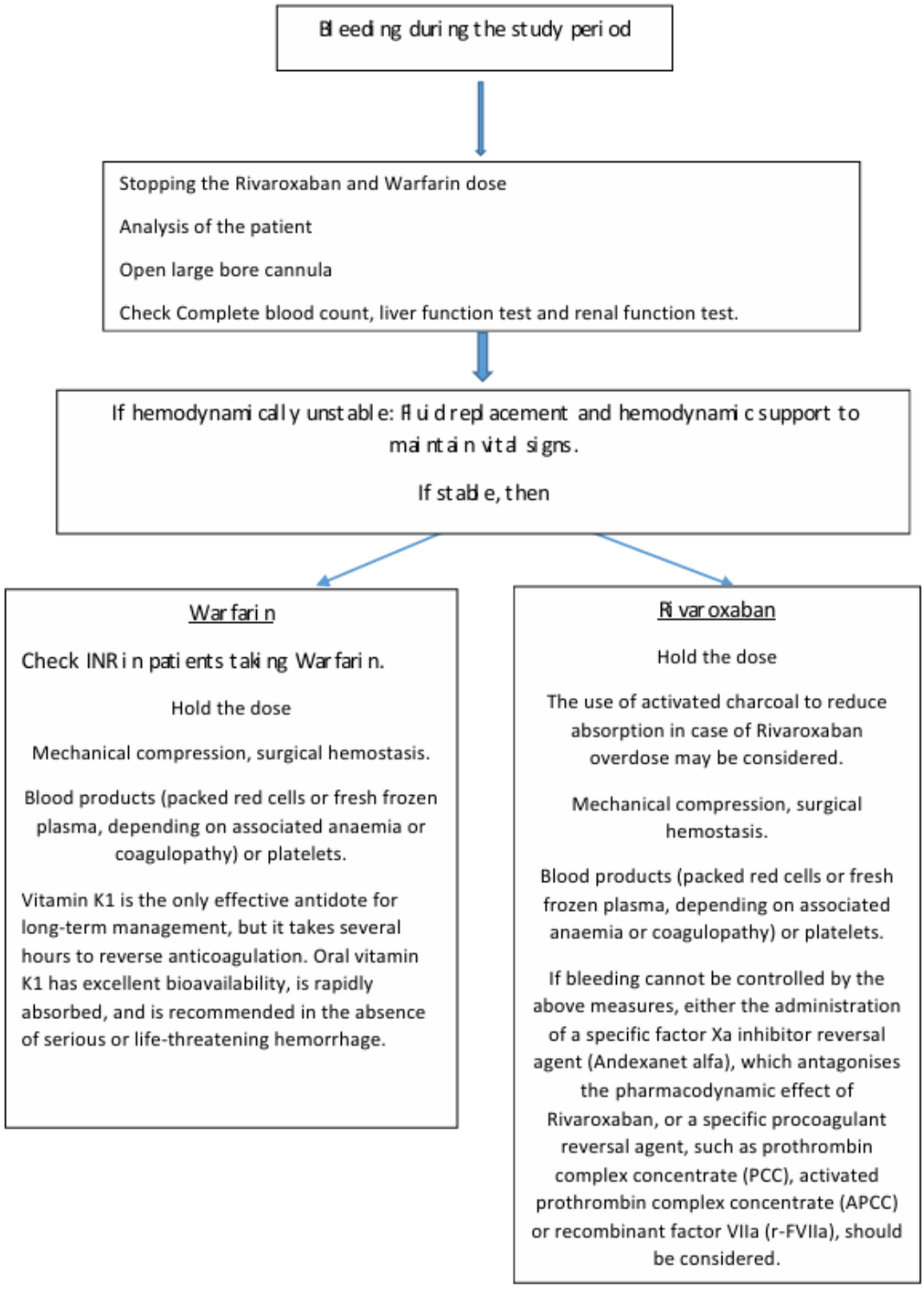
2. Dr. Nivesh Rajbhandari
Registrar
Department of Cardiovascular Surgery
Member: Institutional Review Committee
Shahid Gangalal National Heart Center
niveshraj@hotmail.com, 9851098400

3. Dr. Battu Kumar Shrestha
Cardiac Anesthesiologist
Department of Cardiac Anestheia
Shahid Gangalal National Heart Center
battushrestha@gmail.com, 9851144822

Roles and responsibility of DSMB

1) To review and evaluate the accumulated study data at the end of one third of the participant or end of every month whichever is earlier for
- participant safety
- study conduct and progress
- efficacy

2) Make recommendations concerning the continuation, modification, or termination of the trial.


Bleeding during the study period
Stopping the Rivaroxaban and Warfarin dose
Analysis of the patient
Open large bore cannula
Check Complete blood count, liver function test and renal function test.
If hemodynamically unstable: Fluid replacement and hemodynamic support to maintain vital signs.
If stable, then
Warfarin
Check INR in patients taking Warfarin.
Hold the dose
Mechanical compression, surgical hemostasis.
Blood products (packed red cells or fresh frozen plasma, depending on associated anaemia or coagulopathy) or platelets.
Vitamin K1 is the only effective antidote for long-term management, but it takes several hours to reverse anticoagulation. Oral vitamin K1 has excellent bioavailability, is rapidly absorbed, and is recommended in the absence of serious or life-threatening hemorrhage.
Rivaroxaban
Hold the dose
The use of activated charcoal to reduce absorption in case of Rivaroxaban overdose may be considered.
Mechanical compression, surgical hemostasis.
Blood products (packed red cells or fresh frozen plasma, depending on associated anaemia or coagulopathy) or platelets.
If bleeding cannot be controlled by the above measures, either the administration of a specific factor Xa inhibitor reversal agent (Andexanet alfa), which antagonises the pharmacodynamic effect of Rivaroxaban, or a specific procoagulant reversal agent, such as prothrombin complex concentrate (PCC), activated prothrombin complex concentrate (APCC) or recombinant factor VIIa (r-FVIIa), should be considered.

अध्ययन शीर्षक :	**Comparison of Warfarin versus Rivaroxaban in management of post-myocardial infarction left ventricular thrombus in a tertiary cardiac center of Nepal: A Randomized control study.**
स्थानीय चिकित्सक :	Dr. Dipanker Prajapati
प्रायोजक :	शहिद गंगालाल राष्ट्रिय हृदय केन्द्र

सहभागी जानकारी पत्र र सूचित सहमती मञ्जुरी फारम

आपतकालिन सम्पर्क नं (२४ घन्टा / ७ दिन) : 977-9849273202

नेपाल स्वास्थ्य अनुसन्धान परिषद (NHRC)को सम्पर्क नं 977-1-4254220

आपतकालिन सम्पर्क नं यस पत्रको अन्तिम पृष्ठमा "सम्पर्क नं"नामक शिर्षकमा उल्लेख गरिएकोछ ।

परिचय

तपाईलाई भर्खरै हृदयघात भएको थियो र हृदयघात भएको समय लामो भएको कारणले तपाइको मुटुको मांसपेसीहरुको मृत्यु भएको र सो कारणले मुटुको ठुलो भागले काम गर्न छोडेको छ। सो काम नगरेको मुटुको भागमा Cardiac MRI परिक्षण द्वारा तपाइको मुटुभित्र रगत जमेको पुस्टि भएको छ। यस्तो मुटु भित्र रगत जम्दा खेरि कुनै पनि बेला त्यो जमेको रगत उछिटिएर शरीरको विभिन्न अंगमा पुगेर त्यहाँको रक्त संचारमा वाधा पुर्याउन सक्छ। जसकारणले तपाइलाई मस्तिस्कघात, अन्धोपना जस्ता भयानक जटिल रोगहरुको सम्भावना हुनुको साथसाथै विभिन्न अंगहरु काट्नु पर्ने जटिलताको पनि सम्भावना हुन सक्छ।

संसारभर यस्तो रोगमा warfarin नामक रगत पगाल्ने औषधिको प्रयोग गर्ने गरिन्छ। तर Warfarin को प्रयोग गर्दाखेरि सबै बिरामीहरुले यति नै dose भन्ने हुँदैन। Warfarin को dose मानिस मानिस अनुसार फरक हुने र कसैलाई कम dose चाहिने हुन्छ भने कसैलाई धेरै dose को प्रयोग गर्नु पर्ने हुन्छ। साथै धेरै dose को प्रयोग हुँदा धेरै रगत पग्लिएर रक्तश्राव को जटिलता पनि हुनसक्छ। Warfarin को प्रयोग गर्दा सुरुमा रगत कति पातलो भएको छ भनेर रगतको जांच गर्ने र सो जाँच पटक पटक गर्नु पर्ने हुन्छ।

अहिले नयाँ औसधि Rivaroxaban आएको छ जसमा पटक पटक रगतको जांच गर्नुपर्ने झन्झट नहुने साथै सबैलाई एउटै dose प्रयोग हुने भएकोले सजिलो हुने गर्छ।

नेपाल जस्तो देशमा पटक पटक रगत परिक्षण गर्दा अस्पताल आउनेजाने खर्च, पटक पटक रगत परिक्षण को खर्च अलि कम हुन्छ।

यधपि Warfarin र Rivaroxaban औषधिको जटिलता Bleeding अथवा रक्तश्राव हुने सम्भावना हो ।

तपाईलाई यस अध्धयनमा सहभागी हुन निम्त्याइएको हो । यस मन्जुरीनामा फारमबाट तपाईले जानकारी लिईआफ्नो निर्णयदिन सक्नुहुन्छ । कृपया यस फारम पढेर केहि प्रश्न भए सोध्नु होला । तपाईले आफ्ना सबै प्रश्नको उत्तर पाउनुपर्छ । यस अध्ययनका चिकित्सक/कर्मचारीले तपाईलाई यो अध्ययनको समय सिमाबारे बताउनु हुन्छ जसले गर्दा तपाईलाई आफ्नो निर्णय गर्न मद्दत हुन्छ । यो अध्ययनमा भाग लिने नलिने तपाईको स्वइच्छा हो ।अध्ययनमा सहभागी भएर पछि आफ्नो सहभागीताबाट हट्ने निर्णयले तपाईलाई कुनैपनि जरिवाना वा अहिले र भविष्यमा पाउने स्वास्थ्य सुविधामा बाधा आउने छैन ।

अध्ययनमा सहभागीहरुको के के जिम्मेवारी हुनेछ ?

यस अध्ययनमा सहभागीता लिने भए, तपाईबाट निम्न बुंदा अनुसार आशा गरिन्छ :-

- आफ्नो डाक्टरलाई अहिले कुनै रोग भएमा जानकारी दिनुहोस
- आफुले खाने प्रेसकृप्सन वा बाहिरको औषधी र सप्लिमेन्टस् (जडिबुटि वा भिटामिन) सुरु गर्नु, बन्द गर्नु वा परिवर्तन गर्नु अघि डाक्टरको सल्लाह लिनुहोस्। यो तपाईको, अध्ययनका बेला खाईरहेको औषधीसँग नजुधोस भनेर हो ।
- यदि अरु अध्ययनमा सहभागी हुने विचार भए, अध्ययनमा संलग्न चिकित्सकलाई भन्नुहोस ।
- प्रयोग नभएका औषधीहरु फिर्ता गर्नुहोस ।
- तपाई गर्भवती भए वा तपाई पुरुष भएको खण्डमा बुवा हुने भए अध्ययनमा संलग्न चिकित्सकलाई खबर गर्नु होला ।
- तपाईको औषधी अरुसँग नबाँड्नु होस्। यो औषधी तपाईको लागी मात्र हो ।

सहभागीहरु यस अध्ययन र अनुसन्धानमा कति समय रहनुहुन्छ ?

यस अध्ययन अनुसन्धानमा उपचार विधि तिन महिनामा सक्छ । तपाईको अध्ययनमा सहभागी भएको समयले यस अवधिलाई फरक पार्छ ।

- ३ दिन देखि १४ दिन
  यस अवधिमा तपाईले रगतको जाँचको लागी, अस्पतालबाट डिस्चार्ज भएपछि आउनु पर्ने हुन्छ । रगत संकलन गर्ने स्थानबारे अध्ययन कर्मचारीले जानकारी दिनेछन् ।
- ३ महिना
  यस अवधिमा तपाईले अध्ययन अनुगमनको लागी अस्पताल गई डाक्टर वा अध्ययनको कर्मचारीलाई भेट्नुपर्नेछ । तपाईको आवश्यक जाँच, स्वास्थ्य मूल्यांकन, औषधीको समिक्षा र रगतको जाँच गरिनेछ । र Cardiac MRI को जाँच गरेर पुन: मुटु भित्र जमेको रगत छ वा छैन भनेर मुल्यांकन गरिन्छ।

के सहभागीहरुले यस अध्ययन र अनुसन्धान छोड्न पाउनेछन् ?

सहभागीहरुले यस अध्ययनमा सहभागीता कुनैपनि बेला कारण नखुलाईकन छोड्न सक्छन् । यस अध्ययनबाट आफ्नो सहभागीता

रद्द गर्नुअघि लिईएको तपाई सम्बन्धि जानकारी अनुसन्धानकर्ताहरुले अध्ययनमा प्रयोग गर्न सक्नेछन् तर रद्द गरे पश्चात केहि जानकारी संकलन गर्न वा पठाइने छैन ।

यदि यस्तो भएमा, सहमति पत्रमा उल्लेख भए पनि तपाईले पूर्ण अवधिको लागीऔषधी पाउनु हुने छैन । तपाई यस अध्ययनबाट हटाइए पनि अध्ययन चिकित्सकले तपाई सँग कारणहरुको बारेमा छलफल गर्नुहुनेछ र तपाईको निरन्तर हेरचाहको लागी छुट्टै योजनाहरु बनाउनुहुनेछ ।

यस अध्ययनमा सहभागी हुंदाका जोखिम वा हानीहरु के के छन् ?

तपाई यस अध्ययनमा सहभागीहुँदा केही जोखिमहरु हुन्छन् । यो औषधीका केही जोखिमहरु छन् । येधपि Warfarin र Rivaroxaban औसधिको जटिलता भनेको एउटै हो जुन हो Bleeding अथवा रक्तश्राव हुने सम्भावना।

अध्ययन चिकित्सकले हानी हुन्छ/हुदैन भनि निगरानी गर्नु हुन्छ। आवश्यक परेमा त्यस साइड इफेक्ट कम गर्न र सहज बनाउन अन्य औषधीको प्रयोगको लागी सुझाईन पनि सकिनेछ । प्राय साइड इफेक्ट अध्ययनको समय पछि सकिन्छ तर कुनै साइड इफेक्ट खतराजनक, लामो समय रहने वा मृत्युको कारक पनि हुने सम्भावना हुन्छ ।

यदि तपाईलाई गम्भीर साइड इफेक्टका लागी उपचार जरुरी भएमा, तपाईले अध्ययन औषधी पाउनु भएकै अस्पतालमा आउने प्रयत्न गर्नुपर्छ । अस्पताल आउन नसक्ने खण्डमा कृपया अध्ययन चिकित्सकलाई सम्पर्क गर्नुहोला ।

यस अध्ययनमा भाग लिदा हुने लाभहरु के हुन् ?

यस अध्ययनमा भाग लिदा यस अध्ययनमा प्रयोग हुने औषधी निशुल्क प्राप्त गर्ने बाहेक तपाईलाई अरु प्रत्यक्ष फाइदाहरु हुने छैन । यस अध्ययनको नतिजाबाट भोलिको दिनमा हृदयघात भएर मुटुभित्र रगत जमेको बिरामीहरुको उपचारमा फाइदा हुने आशा गर्दछौं ।

सहभागी जानकारी पत्र कसरी गोप्य राखिनेछ ?

यदि तपाई यस अध्ययनमा सहभागी हुनु भएमा अध्ययन चिकित्सक, अध्ययन कर्मचारीले यस अध्ययनमा चाहिने मात्र जानकारी संकलन गर्नेछन् । सबै जानकारीहरु गोप्य रहनेछन् र लाग्ने कानुनहरु र/वा नियमहरुद्धारा अनुमती दिइएको हदसम्म सार्वजनिक रुपमा उपलब्ध हुने छैन । निम्न संगठनहरुका आधिकारिक प्रतिनिधिहरुले यस अध्ययनको लागी संकलन गरिएको जानकारी सही छ र उचित कानुन र दिशानिर्देशहरु पालना गरिएको छ भनि जाँच गर्न तपाईको सक्कल (पहिचान खुल्ने) मेडिकल र क्लिनिकल अध्ययन रेकर्डहरु हेर्न सक्छन् ।

- अनुसन्धानको नैतिक आचरणको निरीक्षण गर्ने विभाग

मानिसमा गरिने अनुसन्धानमा आफ्नो जात र समप्रदाय (Ethnicity) लगायत अन्य गुणहरुको जानकारी दिन आवश्यक हुन्छ किनभने त्यसले उपचारविधिको नतिजालाई फरक पारिरहेको हुनसक्छ । त्यसकारण आफ्नो जात र समप्रादय बारे जानकारी दिन जरुरी हुन्छ ।

यस अध्ययनको नतिजा सार्वजनिक भएता पनि तपाईको पहिचान गोप्य रहनेछ । यस अध्ययनमा लिइएको तथ्यांक कुनै वैज्ञानिक समुदायको गोष्ठी या जरनलमा सार्वजनिक गर्न सकिन्छ ।

यस अध्ययनको तथ्यांकबाट तपाईलाई पहिचान गर्ने संभावना निम्न भएपनि पुरै शुन्य भने हुदैन ।

यस अध्ययनमा तपाईले सहि गर्नुभएको सहभागीताको प्रतिलिपिमा तपाईको स्वास्थ्य रेकर्ड/अस्पताल पत्र हुनसक्छन् ।

यस अध्ययन संयुक्त राज्य अमेरिकाको नियमनमा (Regulations)पर्ने भएकाले, यस अध्ययनभर हुने विषय फुड एन्ड ड्रग एडमिनिस्ट्रेसन (एफ.डि.ए.) ले तथ्यांकको प्रतिलिपि लिनसक्छ जसमा तपाइको व्यक्तिगत जानकारी हुनसक्छ । यस अध्ययनका डाक्टरले सकेसम्म तपाईलाई यस सहमतिको जानकारी दिनुहुन्छ । त्यसमा सहि गरे, तपाईले तथ्यांक सार्वजनिक गर्ने अनुमति दिनुभएको हो । गोपनियताका नियमहरु देश-देश विचमा फरक पर्न सक्छन् ।

के तपाईको आफ्नो चिकित्सकलाई तपाईको यस अध्ययनमा सहभागीताको जानकारी हुन्छ ?

तपाईको चिकित्सकलाई यस अध्ययनमा सहभागीतावारे जानकारी गराउन सक्नुहुन्छ । यदि जानकारी दिन मन नभएको खण्डमा, यस अध्ययन टिमलाई जानकारी दिनुहोला ।

के यस अध्ययनको बारेमा जानकारी अनलाइन उपलब्ध हुनेछ ?

यस क्लिनिकल परीक्षणको विवरण http://clinicaltrials.govमा **NCT05794399 मा** उपलब्ध हुनेछ । यो वेबसाइटले तपाइलाई पहिचान गर्ने सक्ने जानकारी समावेश गर्दैन । तपाई कुनै पनि समय यो वेबसाइट खोज्न सक्नुहुन्छ ।

सहभागीहरुलाई के लागत छ ?

यस अध्ययनमा Warfarin र Rivaroxaban निशुल्क वितरण गरिनेछ ।

यस अध्ययनमा भाग लिएमा तपाईलाई अन्य अतिरिक्त खर्च लाग्न सक्छ, जस्तै :-

- सहभागी हुने दिनको तपाईको काम छुट्न सक्ने

तर तपाईको यस विधिको अतिरिक्त शुल्कलाई जस्तै कुनै साइड इफेक्टको उपचार गर्न र औषधी किन्नु परेमा यस अध्ययनले खर्चको व्यवस्था गर्नेछ ।

यस अनुसन्धान अध्ययनमा सहभागीहरुको अधिकारहरु के हुन्छन् ?

समय समयमा तपाईको सहभागीताको मन्जुरीलाई फरक पार्न सक्ने जानकारी गराइन्छ ।

अध्ययन सकिएपछि यसको नतिजाबारे जानकारी पाउनु तपाईको अधिकार हो । नेपालको कानुन बमोजिम तपाईको गोपनियताको सुरक्षा गरिएको हुन्छ ।

यस मन्जुरी फारममा हस्ताक्षर गरेर नेपालको कानुन अर्न्तगत तपाईले प्राप्त गर्ने कुनै पनि कानुनी अधिकारलाई तपाईले परित्याग गर्नुहुने छैन र यसको अर्थ तपाईले अध्ययन चिकित्सक, उनीहरुको संस्था वा प्रायोजकलाई उनीहरुको कानुनी तथा व्यावसायिक जिम्मेवारीबाट मुक्त गर्दै हुनुहुन्छ भन्ने होइन ।

तपाईलाई अध्ययन अघि सहि गर्नुभएको मितिको मञ्जुरीनामाको प्रतिलिपि दिइने छ ।

सहभागीहरुले आफ्ना प्रश्नहरुका लागी कस्लाई सम्पर्क गर्न सक्छन् ?

यस अध्ययन नेपाल स्वास्थ्य अनुसन्धान परिषद (NHRC)ले समिक्षा गरेको हो । आफ्नो सहभागीता वापत तपाईको केहि प्रश्न भएमा, कृपया नेपाल स्वास्थ्य अनुसन्धान परिषद (NHRC)को सम्पर्क नं 977-1-4254220 मा सम्पर्क गर्नुहोला । माथी उल्लेखित डाक्टर र फोन नम्बरमा पनि सम्पर्क गर्नु होला।

हस्ताक्षरहरु:-

- मेरा सबै प्रश्नको उत्तर पाएको छु ,
- यस मञ्जुरीनामा रहेको सबै बुंदाबारे जानकार छु ,
- म मेरो स्वास्थ्यबारे जानकारी यस मञ्जुरीनामा उल्लेख भएझै खुलाउन सहमत छु ,
- यस मञ्जुरीनामामा सहि गरेवापत म कुनै कानुनी अधिकारबाट बञ्चित हुने छैन ,
- मेरो चिकित्सकलाई मेरो स्वास्थ्यबारे जानकारी दिन सकिन्छ भन्ने विषयमा म जानकार छु ,
- म यस अध्ययनमा सहभागी हुन्छु,
- मलाई यस मञ्जुरीनामाको प्रतिलिपि दिइन्छ ।

सहभागीको हस्ताक्षर	सहभागीको नाम	मिति
		समय
सहमति प्राप्त गर्ने आधिकारीक व्यक्तिको	नाम र पद	मिति

सहभागीको औंठाछाप (दाँया)	सहभागीको औंठाछाप (बाँया)	मिति
		समय
साक्षीको हस्ताक्षर	साक्षीको नाम	मिति
		समय