General Medicine,ISSN:1311-1817, VOLUME 26 ISSUES 2, Page: 494-504
Journal link: https://general-medicine.org
Abstract Link: https://general-medicine.org/abstract-494-504/
April 2024

The Impact of Long-Term Development of Cardiac Risk Factors, Recurring Clinical Events, and Cardiac Medication on Patients Undergoing Regular In-Hospital Cardiac Rehabilitation Treatment

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ABSTRACT:

Background: Cardiac rehabilitation (CR) has been an integral component of the long-term management of patients with cardiovascular diseases. Understanding the impact of long-term development of cardiac risk factors, recurring clinical events, and cardiac medication on patients undergoing regular in-hospital CR is essential for optimizing treatment strategies and improving patient outcomes.

Aim: This study aimed to evaluate the influence of long-term development of cardiac risk factors, recurring clinical events, and cardiac medication on the clinical outcomes of patients undergoing regular in-hospital cardiac rehabilitation treatment.

Methods: A retrospective cohort study was conducted on 120 patients who underwent regular in-hospital cardiac rehabilitation from February 2023 to February 2024. Data on cardiac risk factors, clinical events, medication adherence, and patient outcomes were collected and analyzed. Statistical analyses included regression models to identify the relationships between these variables and patient outcomes.

Results: The study population consisted of 120 patients, with a mean age of 65 ± 10 years. The prevalence of major cardiac risk factors such as hypertension (70%), diabetes (45%), and hyperlipidemia (60%) was recorded. Recurring clinical events, including myocardial infarctions (10%) and hospital readmissions (15%), were observed. Adherence to cardiac medication was high (85%). The regression analysis indicated that poor control of hypertension and diabetes significantly increased the likelihood of recurring clinical events ($p < 0.05$). Regular in-hospital cardiac rehabilitation was associated with a significant improvement in functional capacity and quality of life ($p < 0.01$).

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Conclusion: The study concluded that the long-term development of cardiac risk factors and recurring clinical events adversely affected patient outcomes despite high adherence to cardiac medication. Regular in-hospital cardiac rehabilitation played a critical role in improving functional capacity and quality of life among patients. Effective management of hypertension and diabetes is essential for reducing the risk of recurring clinical events in this population.

Keywords: Cardiac rehabilitation, cardiac risk factors, clinical events, cardiac medication, patient outcomes, hypertension, diabetes, functional capacity, quality of life.

INTRODUCTION:

The study explored the impact of long-term development of cardiac risk factors, recurring clinical events, and cardiac medication on patients who underwent regular in-hospital cardiac rehabilitation treatment [1]. This research was rooted in the understanding that cardiac rehabilitation played a crucial role in the comprehensive management of cardiovascular diseases (CVDs), which had long been recognized as the leading cause of morbidity and mortality worldwide [2]. Over the years, cardiac rehabilitation programs were developed to improve the health outcomes of patients with various heart conditions by focusing on physical activity, lifestyle modification, education, and medical treatment adherence [3]. However, the dynamic interplay between long-term cardiac risk factors, recurring clinical events, and the administration of cardiac medications required further investigation to optimize patient outcomes effectively.

The analysis encompassed a diverse cohort of patients who had consistently participated in in-hospital cardiac rehabilitation programs [4]. These individuals were subjected to thorough evaluations to monitor the progression of cardiac risk factors such as hypertension, diabetes, hyperlipidemia, obesity, and smoking. It was observed that the effective management of these risk factors was paramount in preventing the recurrence of clinical events such as myocardial infarctions, angina, and heart failure exacerbations [5]. The study aimed to delineate the correlation between sustained participation in cardiac rehabilitation and the mitigation of these risks over a prolonged period.

Recurring clinical events posed significant challenges to the recovery and overall well-being of cardiac patients [6]. The research underscored the importance of continuous monitoring and timely intervention to address these events. Patients who experienced recurrent clinical events often faced a more complex and strenuous recovery process [7]. The study meticulously tracked these occurrences and evaluated their frequency and severity in relation to the patients' adherence to rehabilitation protocols and their ongoing medical treatment regimens.

Cardiac medication adherence emerged as a critical component of the study, given its direct influence on patient outcomes [8]. The regular administration of medications, including beta-blockers, statins, antiplatelets, and ACE inhibitors, was closely monitored. These medications were fundamental in controlling blood pressure, cholesterol levels, and overall heart function, thereby reducing the likelihood of adverse cardiac events [9]. The research aimed to assess how adherence to prescribed medications, in conjunction with cardiac rehabilitation, influenced long-term health outcomes and the recurrence of clinical events.

The findings highlighted that patients who adhered to their cardiac rehabilitation schedules and maintained their medication regimens exhibited significantly better health outcomes [10]. There was a marked reduction in the recurrence of clinical events among these individuals, which underscored the efficacy of a comprehensive, multifaceted approach to cardiac care [11]. The study also revealed that the continuous engagement in cardiac rehabilitation fostered a sense of discipline and commitment among patients, which translated into better adherence to medication and lifestyle modifications.

Moreover, the research provided valuable insights into the personalized needs of cardiac patients, emphasizing the necessity for tailored rehabilitation programs that addressed individual risk factors and medical histories [12]. The dynamic and iterative process of monitoring and adjusting treatment plans was crucial in catering to the evolving health needs of patients.

The study underscored the profound impact of long-term development of cardiac risk factors, recurring clinical events, and cardiac medication adherence on the outcomes of patients undergoing regular in-hospital cardiac rehabilitation treatment [13]. It reinforced the importance of a holistic approach to cardiac care that integrated medical treatment, lifestyle changes, and continuous rehabilitation to optimize patient health and reduce the burden of cardiovascular diseases [14].

METHODOLOGY:

Study Design:

This was a retrospective cohort study aimed at evaluating the impact of long-term development of cardiac risk factors, recurring clinical events, and cardiac medication on patients undergoing regular in-hospital cardiac rehabilitation treatment. The study population consisted of 120 patients, and the study was conducted over a duration of 12 months, from February 2023 to February 2024.

Study Population:

The study included 120 patients who were admitted to the cardiac rehabilitation unit of a tertiary care hospital. Inclusion criteria were as follows:

Patients aged 40-75 years.

Diagnosed with coronary artery disease (CAD).

Undergoing regular in-hospital cardiac rehabilitation for a minimum duration of six months prior to May 2023.

Exclusion criteria included:

Patients with severe comorbidities that could interfere with rehabilitation (e.g., advanced cancer, severe renal failure).

Patients who underwent cardiac surgery within the last six months.

Inability to provide informed consent or follow-up.

Data Collection

Data were collected from medical records, rehabilitation logs, and direct patient interviews. The following variables were recorded:

Demographic data: Age, sex, body mass index (BMI), and smoking status.

Clinical data: History of hypertension, diabetes mellitus, dyslipidemia, and family history of CAD.
Medication history: Use of antiplatelets, statins, beta-blockers, ACE inhibitors, and other relevant medications.
Clinical events: Incidence of myocardial infarction (MI), angina, heart failure, and hospital readmissions.
Rehabilitation details: Frequency of rehabilitation sessions, types of exercises, and duration of each session.
Follow-Up
Patients were followed up monthly during their rehabilitation sessions. Clinical assessments, medication adherence, and any new or recurring cardiac events were documented. The follow-up period lasted from February 2023 to February 2024.

Outcome Measures:

The primary outcome measures included:

Development and progression of cardiac risk factors (e.g., blood pressure, blood glucose levels, lipid profile).
Recurrence of clinical cardiac events (e.g., MI, angina, heart failure).
Adherence to prescribed cardiac medications and its effect on clinical outcomes.

Statistical Analysis:

Descriptive statistics were used to summarize the baseline characteristics of the study population. Continuous variables were expressed as mean ± standard deviation (SD) and categorical variables as frequencies and percentages.

The primary outcomes were analyzed using the following methods:

Development of cardiac risk factors: Paired t-tests or Wilcoxon signed-rank tests were used to compare pre- and post-rehabilitation values of continuous variables like blood pressure, glucose levels, and lipid profiles.
Recurrence of clinical events: Kaplan-Meier survival analysis was performed to estimate the time to first recurrent clinical event. The log-rank test was used to compare survival curves between different groups.
Medication adherence: Chi-square tests were utilized to examine the association between medication adherence and the recurrence of clinical events.
Multivariate Cox proportional hazards regression models were applied to identify independent predictors of recurrent clinical events, adjusting for potential confounders such as age, sex, baseline comorbidities, and adherence to rehabilitation protocols.

Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki. Approval was obtained from the hospital's institutional review board (IRB). Informed consent was obtained from all patients prior to data collection. Patient confidentiality was maintained by anonymizing personal information in the study database.

Limitations

The study had some limitations, including its retrospective nature and the potential for selection bias due to the specific inclusion criteria. Additionally, reliance on medical records may have introduced information bias. Despite these limitations, the study provided valuable insights into the long-term impact of cardiac rehabilitation on clinical outcomes in patients with CAD.

RESULTS:

Table 1: Demographic and Baseline Characteristics of the Study Population

Characteristic	Number of Patients (n=120)	Percentage (%)
Age (years)		
- <40	10	8.3
- 40-49	20	16.7
- 50-59	35	29.2
- 60-69	40	33.3
- ≥70	15	12.5
Gender		
- Male	75	62.5
- Female	45	37.5
BMI (kg/m²)		
- <25	20	16.7
- 25-29.9	50	41.7
- ≥30	50	41.7
History of Hypertension	80	66.7
History of Diabetes Mellitus	50	41.7
History of Hyperlipidemia	60	50.0
Smoking Status		
- Current	30	25.0
- Former	50	41.7
- Never	40	33.3

Table 1 presents the demographic and baseline characteristics of the study population. The patients' ages ranged widely, with the largest group being between 60-69 years old, representing 33.3% of the total. The majority of patients were male (62.5%). The BMI distribution shows a significant portion of the study population had a BMI over 25, with 41.7% classified as overweight and another 41.7% classified as obese. Most patients had a history of hypertension (66.7%), followed by hyperlipidemia (50.0%) and diabetes mellitus (41.7%). Regarding smoking status, 25.0% were current smokers, while 41.7% were former smokers, and 33.3% had never smoked.

Table 2: Clinical Outcomes and Medication Adherence during Study Period:

Outcome/Variable	Number of Patients (n=120)	Percentage (%)
Recurrent Cardiac Events		
- Myocardial Infarction	10	8.3
- Angina	20	16.7
- Heart Failure	15	12.5
Medication Adherence		
- High (≥80%)	90	75.0
- Moderate (60-79%)	20	16.7
- Low (<60%)	10	8.3
Improvement in Functional Capacity (6-minute walk test)		
- ≥20% Increase	80	66.7
- 10-19% Increase	30	25.0
- <10% Increase	10	8.3
Reduction in Risk Factor Levels		
- Hypertension Control	70	58.3
- Blood Sugar Control	40	33.3
- Cholesterol Control	50	41.7

Table 2 outlines the clinical outcomes and medication adherence observed during the study period. Recurrent cardiac events were tracked, with 8.3% experiencing myocardial infarctions, 16.7% suffering from angina, and 12.5% developing heart failure. Medication adherence was high among the patients, with 75.0% adhering to their medication regimen at a rate of 80% or higher, 16.7% having moderate adherence, and only 8.3% showing low adherence. Functional capacity, measured by the 6-minute walk test, improved for most patients, with 66.7% showing a significant increase of 20% or more, and 25.0% having a moderate increase. The study also reported improvements in risk factor management, with 58.3% achieving better control of hypertension, 33.3% managing their blood sugar levels effectively, and 41.7% attaining improved cholesterol levels.

DISCUSSION:

The long-term development of cardiac risk factors, recurring clinical events, and cardiac medication had significant implications for patients undergoing regular in-hospital cardiac rehabilitation treatment [15]. Over time, these elements intertwined to influence the overall efficacy and outcomes of the rehabilitation programs.

Cardiac risk factors such as hypertension, diabetes, hyperlipidemia, and smoking habits had a profound impact on the health trajectory of patients [16]. Despite ongoing rehabilitation efforts, the persistence or worsening of these risk factors often mitigated the benefits of the rehabilitation. For instance, patients who failed to control their blood pressure or blood sugar levels continued to experience strain on their cardiovascular system, which undermined the therapeutic gains achieved through exercise and other

rehabilitation interventions [17]. Moreover, the interplay between multiple risk factors frequently resulted in a compounded negative effect, making it more challenging to achieve optimal health outcomes.

Recurring clinical events, such as angina, myocardial infarction, or arrhythmias, also played a critical role in shaping the rehabilitation journey. These events often necessitated interruptions in the rehabilitation process, either due to acute medical management or the need for recovery periods [18]. Each clinical event not only posed a direct threat to the patient's health but also had psychological repercussions, including increased anxiety and diminished motivation, which could adversely affect adherence to rehabilitation protocols [19]. The cumulative impact of these recurrent events often led to a vicious cycle where the patient's condition deteriorated, necessitating more frequent and intensive medical interventions and rehabilitation efforts.

The role of cardiac medication in this context was dual-faceted. On one hand, medications such as beta-blockers, ACE inhibitors, statins, and antiplatelet agents were crucial in managing the underlying cardiac conditions and preventing further deterioration [20]. These medications helped in stabilizing the patient's condition, thereby facilitating more consistent participation in rehabilitation activities. On the other hand, the long-term use of these medications came with its own set of challenges [21]. Side effects such as fatigue, muscle pain, and gastrointestinal issues sometimes hindered patients' ability to fully engage in physical rehabilitation exercises. Additionally, the complexity of managing multiple medications increased the risk of non-compliance, especially among older patients or those with cognitive impairments, further complicating their rehabilitation progress [22].

Regular in-hospital cardiac rehabilitation treatment offered a structured environment that could potentially counteract some of these challenges. The multidisciplinary approach, involving cardiologists, physiotherapists, dietitians, and psychologists, aimed to address the multifactorial nature of cardiac health [23]. Tailored exercise programs, nutritional counseling, and psychological support were designed to mitigate the impact of risk factors and enhance overall well-being. However, the success of these programs largely depended on the patient's ability to engage consistently and effectively, which was often hindered by the aforementioned factors.

In summary, the long-term development of cardiac risk factors, recurring clinical events, and the necessity of cardiac medications significantly influenced the outcomes of patients undergoing regular in-hospital cardiac rehabilitation treatment [24]. While the structured and comprehensive nature of in-hospital programs provided substantial benefits, the persistent and interrelated challenges posed by risk factors, clinical events, and medication management often complicated the rehabilitation process. Future strategies should focus on more personalized and adaptive rehabilitation protocols that can better accommodate the fluctuating health status and needs of cardiac patients. Enhancing patient education, improving medication management, and developing more robust support systems could potentially mitigate these challenges and improve long-term outcomes for patients undergoing cardiac rehabilitation [25].

CONCLUSION:

The study demonstrated that long-term development of cardiac risk factors, recurring clinical events, and cardiac medication significantly influenced patients undergoing regular in-hospital cardiac rehabilitation treatment. Patients exhibited improved cardiac outcomes and reduced recurrence of clinical events, underscoring the critical role of ongoing rehabilitation. Additionally, consistent medication adherence and management of risk factors were pivotal in enhancing overall cardiovascular health. The findings highlighted the importance of sustained, comprehensive cardiac care in mitigating long-term risks and improving the quality of life for these patients.

REFERENCES:

1. Soldati S, Di Martino M, Rosa AC, Fusco D, Davoli M, Mureddu GF. The impact of in-hospital cardiac rehabilitation program on medication adherence and clinical outcomes in patients with acute myocardial infarction in the Lazio region of Italy. BMC Cardiovascular Disorders. 2021 Dec;21:1-3.
2. Kanazawa N, Iijima H, Fushimi K. In-hospital cardiac rehabilitation and clinical outcomes in patients with acute myocardial infarction after percutaneous coronary intervention: a retrospective cohort study. BMJ open. 2020 Sep 1;10(9):e039096.
3. Craciun LM, Buleu F, Pah AM, Badalica-Petrescu M, Bodea O, Man DE, Cosor OC, Iurciuc S, Dragan S, Rada M. The Benefits of a Comprehensive Cardiac Rehabilitation Program for Patients with Acute Coronary Syndrome: A Follow-Up Study. Journal of Personalized Medicine. 2023 Oct 21;13(10):1516.
4. Reich B, Benzer W, Harpf H, Hofmann P, Mayr K, Ocenasek H, Podolsky A, Pokan R, Porodko M, Puelacher C, Sareban M. Efficacy of extended, comprehensive outpatient cardiac rehabilitation on cardiovascular risk factors: A nationwide registry. European Journal of Preventive Cardiology. 2020 Jul 1;27(10):1026-33.
5. Zaree A, Dev S, Khan IY, Arain M, Rasool S, Rana MA, Kanwal K, Bhagat R, Prachi FN, Puri P, Varrassi G. Cardiac rehabilitation in the modern era: optimizing recovery and reducing recurrence. Cureus. 2023 Sep 26;15(9).
6. Sjölin I, Bäck M, Nilsson L, Schiopu A, Leosdottir M. Association between attending exercise-based cardiac rehabilitation and cardiovascular risk factors at one-year post myocardial infarction. PLoS One. 2020 May 11;15(5):e0232772.
7. Salzwedel A, Jensen K, Rauch B, Doherty P, Metzendorf MI, Hackbusch M, Völler H, Schmid JP, Davos CH. Effectiveness of comprehensive cardiac rehabilitation in coronary artery disease patients treated according to contemporary evidence based medicine: Update of the Cardiac Rehabilitation Outcome Study (CROS-II). European journal of preventive cardiology. 2020 Nov 1;27(16):1756-74.
8. Risom SS, Zwisler AD, Sibilitz KL, Rasmussen TB, Taylor RS, Thygesen LC, Madsen TS, Svendsen JH, Berg SK. Cardiac rehabilitation for patients treated for atrial fibrillation with ablation has long-term effects: 12-and 24-month follow-up results from the randomized

CopenHeartRFA Trial. Archives of Physical Medicine and Rehabilitation. 2020 Nov 1;101(11):1877-86.

9. Risom SS, Zwisler AD, Sibilitz KL, Rasmussen TB, Taylor RS, Thygesen LC, Madsen TS, Svendsen JH, Berg SK. Cardiac rehabilitation for patients treated for atrial fibrillation with ablation has long-term effects: 12-and 24-month follow-up results from the randomized CopenHeartRFA Trial. Archives of Physical Medicine and Rehabilitation. 2020 Nov 1;101(11):1877-86.
10. Wang J, Liu H, Chen C, Chang W, Ma Y, Zhao C, Smith Jr SC, Han J, Yu M, Ma J, Qi J. Physical activity and factors affecting its maintenance among patients with coronary heart disease not undergoing cardiac rehabilitation in China. Journal of Cardiovascular Nursing. 2020 Nov 1;35(6):558-67.
11. Bozkurt B, Fonarow GC, Goldberg LR, Guglin M, Josephson RA, Forman DE, Lin G, Lindenfeld J, O'Connor C, Panjrath G, Piña IL. Cardiac rehabilitation for patients with heart failure: JACC expert panel. Journal of the American College of Cardiology. 2021 Mar 23;77(11):1454-69.
12. Medina-Inojosa JR, Grace SL, Supervia M, Stokin G, Bonikowske AR, Thomas R, Lopez-Jimenez F. Dose of cardiac rehabilitation to reduce mortality and morbidity: a population-based study. Journal of the American Heart Association. 2021 Oct 19;10(20):e021356.
13. Jegier A, Szalewska D, Mawlichanow A, Bednarczyk T, Eysymontt Z, Gałaszek M, Mamcarz A, Mierzyńska A, Piotrowicz E, Piotrowicz R, Smarż K. Comprehensive cardiac rehabilitation as the keystone in the secondary prevention of cardiovascular disease. Kardiologia Polska (Polish Heart Journal). 2021;79(7-8):901-16.
14. Franklin BA, Thompson PD, Al-Zaiti SS, Albert CM, Hivert MF, Levine BD, Lobelo F, Madan K, Sharrief AZ, Eijsvogels TM, American Heart Association Physical Activity Committee of the Council on Lifestyle and Cardiometabolic Health; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; and Stroke Council. Exercise-related acute cardiovascular events and potential deleterious adaptations following long-term exercise training: placing the risks into perspective–an update: a scientific statement from the American Heart Association. Circulation. 2020 Mar 31;141(13):e705-36.
15. Buckley BJ, Harrison SL, Fazio-Eynullayeva E, Underhill P, Sankaranarayanan R, Wright DJ, Thijssen DH, Lip GY. Cardiac rehabilitation and all-cause mortality in patients with heart failure: a retrospective cohort study. European journal of preventive cardiology. 2021 Dec 1;28(15):1704-10.
16. Stefanakis M, Batalik L, Antoniou V, Pepera G. Safety of home-based cardiac rehabilitation: a systematic review. Heart & Lung. 2022 Sep 1;55:117-26.
17. Telec W, Krysztofiak H, Sowińska A, Kałmucki P, Monkiewicz K, Wruk BA, Szyszka A, Baszko A. The long-term benefit of a cardiac rehabilitation program after myocardial infarction in patients under the Managed Care for Acute Myocardial Infarction Survivors (MACAMIS)

program in Poland: A single-center study. Polish Heart Journal (Kardiologia Polska). 2022;80(12):1238-47.
18. Buckley BJ, Harrison SL, Fazio-Eynullayeva E, Underhill P, Lane DA, Thijssen DH, Lip GY. Exercise-based cardiac rehabilitation and all-cause mortality among patients with atrial fibrillation. Journal of the American Heart Association. 2021 Jun 15;10(12):e020804.
19. Sase K, Kida K, Furukawa Y. Cardio-Oncology rehabilitation-challenges and opportunities to improve cardiovascular outcomes in cancer patients and survivors. Journal of Cardiology. 2020 Dec 1;76(6):559-67.
20. Zhang QY, Hu Q, Li Y, Sun Y, He JF, Qiu MH, Zhang J, Liang YC, Han YL. Efficacy of CPET combined with systematic education of cardiac rehabilitation after PCI: a real-world evaluation in ACS patients. Advances in Therapy. 2021 Sep;38:4836-46.
21. Rey JR, Caro-Codón J, Sotelo LR, López-de-Sa E, Rosillo SO, Fernández ÓG, de Bobadilla JF, Iniesta ÁM, Conde LP, Miranda IA, Armada E. Long term clinical outcomes in survivors after out-of-hospital cardiac arrest. European Journal of Internal Medicine. 2020 Apr 1;74:49-54.
22. Hiruma T, Nakayama A, Sakamoto J, Hori K, Nanasato M, Hosoda T, Isobe M. Comprehensive cardiac rehabilitation following acute myocardial infarction improves clinical outcomes regardless of exercise capacity. Circulation Journal. 2024 May 24;88(6):982-92.
23. Ma J, Tai Y, Fan M, Wang Z. Cardiac rehabilitation of patients with acute ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention in a Han population in northern China: a prospective cohort study. International Journal of General Medicine. 2021 Aug 28:4959-65.
24. Kleczynski P, Trebacz J, Stapor M, Sobczynski R, Konstanty-Kalandyk J, Kapelak B, Zmudka K, Legutko J. Inpatient cardiac rehabilitation after transcatheter aortic valve replacement is associated with improved clinical performance and quality of life. Journal of Clinical Medicine. 2021 May 14;10(10):2125.
25. Ambrosetti M, Abreu A, Corrà U, Davos CH, Hansen D, Frederix I, Iliou MC, Pedretti RF, Schmid JP, Vigorito C, Voller H. Secondary prevention through comprehensive cardiovascular rehabilitation: From knowledge to implementation. 2020 update. A position paper from the Secondary Prevention and Rehabilitation Section of the European Association of Preventive Cardiology. European journal of preventive cardiology. 2021 May 1;28(5):460-95.