



Bivalirudin for anticoagulation in elderly acute coronary syndrome: Effects on myocardial microcirculation and adverse events

Chun-Yao Cheng, Wen-Rui Hao, Tzu-Hurng Cheng

Specialty type: Medicine, research and experimental

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification

Scientific Quality: Grade B, Grade B, Grade C, Grade C, Grade D

Novelty: Grade B, Grade B, Grade B, Grade C, Grade C

Creativity or Innovation: Grade B, Grade B, Grade B, Grade C, Grade C

Scientific Significance: Grade B, Grade B, Grade B, Grade C, Grade C

P-Reviewer: Barison A; Presutti DG; Xue Q

Received: June 15, 2024

Revised: November 8, 2024

Accepted: December 25, 2024

Published online: May 6, 2025

Processing time: 210 Days and 8.4 Hours



Chun-Yao Cheng, Department of Ophthalmology, Cathay General Hospital, Taipei 10633, Taiwan

Chun-Yao Cheng, Department of Medical Education, National Taiwan University Hospital, Taipei 100225, Taiwan

Wen-Rui Hao, Division of Cardiology, Department of Internal Medicine, Shuang Ho Hospital, Ministry of Health and Welfare, Taipei Medical University, New Taipei City 23561, Taiwan

Wen-Rui Hao, Division of Cardiology, Department of Internal Medicine, School of Medicine, College of Medicine, Taipei Medical University, Taipei City 11002, Taiwan

Tzu-Hurng Cheng, Department of Biochemistry, School of Medicine, College of Medicine, China Medical University, Taichung City 404328, Taiwan

Corresponding author: Tzu-Hurng Cheng, PhD, Professor, Department of Biochemistry, School of Medicine, College of Medicine, China Medical University, No. 91 Xueshi Road, North District, Taichung City 404328, Taiwan. thcheng@mail.cmu.edu.tw

Abstract

The management of acute coronary syndrome (ACS) in older patients remains challenging because standard anticoagulants often fail to yield optimal outcomes. Bivalirudin, a direct inhibitor of thrombin, serves as an alternative to traditional therapies. This drug is particularly effective in enhancing myocardial microcirculation and reducing adverse events after clinical interventions. The present article explores the findings of a recent study that highlighted the clinical benefits of bivalirudin by investigating its effects on myocardial microcirculation and adverse cardiac events after percutaneous coronary intervention in older patients with ACS. Compared with unfractionated heparin, bivalirudin markedly reduced the emergency response time and improved cardiac function indicators. It further mitigated the risks of cardiovascular events and recurrent myocardial infarctions. These findings suggest that bivalirudin can enhance myocardial perfusion and reduce bleeding complications, thus serving as a safe, effective anticoagulation agent for older patients with ACS. Nonetheless, further large-scale, high-quality trials are needed to establish optimal usage guidelines and assess long-term outcomes. Integrating bivalirudin into ACS treatment protocols for older patients may help optimize patient care, balancing efficacy and safety. Continual research and consensus building are necessary for the widespread clinical application of bivalirudin and the improvement of ACS outcomes in older patients.

Key Words: Bivalirudin; Acute coronary syndrome; Myocardial microcirculation; Elderly patients; Anticoagulation

©The Author(s) 2025. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: While bivalirudin is more effective than heparin at reducing bleeding events and their associated risks, it has not been conclusively demonstrated to surpass heparin in improving adverse cardiac events during percutaneous coronary intervention (PCI) in elderly patients with acute coronary syndrome (ACS). However, bivalirudin has been shown to enhance myocardial microcirculation and reduce adverse cardiac events following PCI in older patients with ACS. By improving blood flow at the microvascular level and mitigating procedural risks, bivalirudin proves its potential as a superior anticoagulant. It offers a safer and more effective alternative, leading to better clinical outcomes for this high-risk patient population. Thus, bivalirudin emerges as a valuable option in the management of older patients undergoing PCI for ACS.

Citation: Cheng CY, Hao WR, Cheng TH. Bivalirudin for anticoagulation in elderly acute coronary syndrome: Effects on myocardial microcirculation and adverse events. *World J Clin Cases* 2025; 13(13): 98008

URL: <https://www.wjgnet.com/2307-8960/full/v13/i13/98008.htm>

DOI: <https://dx.doi.org/10.12998/wjcc.v13.i13.98008>

TO THE EDITOR

Acute coronary syndrome (ACS) remains a leading cause of morbidity and mortality worldwide, especially among older adults with multiple comorbidities. These patients face increased risks of ischemic and bleeding complications during interventional therapy. Therefore, selecting an optimal anticoagulation strategy during percutaneous coronary intervention (PCI) is crucial for improving outcomes. Historically, unfractionated heparin has been the standard anticoagulant used in PCI. However, recent studies have explored bivalirudin, a direct thrombin inhibitor, as a potentially safer alternative for high-risk groups[1]. Bivalirudin has gained attention for its ability to reduce bleeding events, particularly in elderly patients with ACS. For example, the BRIGHT-4 trial demonstrated that bivalirudin reduced major bleeding events compared to heparin without compromising ischemic outcomes in patients with ST-segment elevation myocardial infarction (STEMI)[2]. Additionally, a systematic review and meta-analysis by Zhang *et al*[3] confirmed that bivalirudin offers a more favorable safety profile regarding bleeding risk while maintaining comparable efficacy in preventing major adverse cardiac events to heparin. These findings suggest that bivalirudin may offer significant advantages for elderly patients who face heightened risks of both thrombosis and bleeding. In this context, the study by Du *et al*[1] provides valuable insights into the effects of bivalirudin on myocardial microcirculation and adverse events following PCI in older ACS patients. By focusing on this vulnerable population, the study adds crucial data to the ongoing discussion on balancing the dual risks of thrombosis and bleeding in PCI. This article will examine the significance of these findings within the current body of evidence and discuss potential implications for clinical practice.

Overview of Du *et al*'s study and significance in elderly ACS patients

Du *et al*[1] address the safety and efficacy of bivalirudin in elderly patients with ACS undergoing PCI, a high-risk group due to comorbidities and increased fragility. The study examines bivalirudin's effects on myocardial microcirculation and adverse events post-PCI, revealing significant enhancements in microvascular flow, crucial for recovery and minimizing ischemic damage in elderly ACS patients. Improved microvascular flow may reduce long-term complications associated with impaired coronary circulation in this vulnerable population. These findings align with broader evidence, such as the BRIGHT-4 trial, which indicated bivalirudin's advantages over heparin in reducing bleeding complications and enhancing perfusion[2]. The significance of Du *et al*'s study[1] is supported by existing literature emphasizing personalized anticoagulation strategies for elderly patients. Zhang *et al*[3] highlighted the importance of minimizing bleeding risks in high-risk populations, as bleeding is a major mortality contributor post-PCI. By showing that bivalirudin can improve microcirculation while reducing adverse events, Du *et al*[1] support its use as a preferred anticoagulant in this group. Furthermore, Du *et al*'s findings contribute to the discussion on balancing ischemic protection and bleeding risks in ACS management[1]. Galli *et al*[4] noted that bivalirudin's direct thrombin inhibition offers a favorable safety profile compared to heparin, especially for high bleeding risk patients. This is particularly relevant for elderly patients who benefit from reduced bleeding and improved coronary flow. In sum, Du *et al*'s research[1] advances our understanding of bivalirudin's benefits for elderly ACS patients and underscores the importance of individualized treatment strategies to optimize outcomes in this high-risk population. By focusing on microcirculatory benefits and adverse event reduction, the study contributes meaningfully to the evolving role of bivalirudin in ACS management.

Comparative effectiveness of bivalirudin vs heparin

Du *et al*[1] compared the effectiveness of bivalirudin and traditional anticoagulants in elderly patients undergoing PCI for ACS, focusing on their unique susceptibility to ischemic and bleeding complications due to diminished renal function and comorbidities. The study found that bivalirudin reduced major bleeding events and significantly improved

myocardial microcirculation. Enhanced microcirculation is crucial for reducing post-PCI adverse outcomes, such as myocardial infarction and stent thrombosis, which are common in elderly populations. These findings align with prior research, including Zhang *et al*[3], which reported lower bleeding risks with bivalirudin compared to heparin in high-risk, older adults. Galli *et al*[4] also emphasized the reduced bleeding complications associated with bivalirudin in ACS patients, highlighting its improved safety profile. Unlike unfractionated heparin, which poses considerable bleeding risks, bivalirudin optimizes microcirculation without compromising safety. This is supported by meta-analyses, such as those by Al-Abdoun *et al*[5], which highlight bivalirudin's bleeding advantages. These findings have important clinical implications, suggesting that bivalirudin may help mitigate traditional trade-offs between efficacy and safety in elderly patients. Overall, Du *et al*'s research[1] underscores the value of bivalirudin in managing elderly ACS patients by offering a safer yet effective alternative to heparin. This study provides critical insights for clinicians aiming to minimize complications in a population particularly vulnerable to both thrombotic and bleeding risks.

Bivalirudin's role in enhancing myocardial microcirculation

Bivalirudin plays a crucial role in improving myocardial microcirculation during PCI, especially in ACS patients. Unlike unfractionated heparin, bivalirudin provides a targeted approach that reduces bleeding risks while optimizing coronary flow. Du *et al*[1] showed that bivalirudin significantly enhances myocardial microcirculation in elderly ACS patients, a group highly susceptible to thrombotic and hemorrhagic complications. Improved microcirculation leads to better myocardial perfusion, reducing adverse events like reinfarction or stent thrombosis. Zhang *et al*[3] further supported bivalirudin's advantages in PCI settings, highlighting its potential superiority over heparin for ACS management. Bivalirudin's mechanism involves direct thrombin inhibition, preventing clot formation and reducing platelet activation and aggregation, thus stabilizing coronary flow dynamics. Research consistently links improved microcirculation with better clinical outcomes, including lower rates of major adverse cardiac events[4]. Supporting bivalirudin's efficacy, Al-Abdoun *et al*[5] reported fewer bleeding complications in patients receiving bivalirudin during PCI compared to those treated with heparin. This reduced bleeding risk, combined with enhanced microcirculation, makes a compelling case for bivalirudin, particularly for older patients with complex medical histories. Additionally, Stone *et al*[2] confirmed bivalirudin's safety and efficacy in STEMI patients, reinforcing its role in improving both microcirculation and overall patient outcomes. In short, bivalirudin is a valuable tool in managing ACS, especially for patients vulnerable to ischemic and bleeding complications. Its ability to improve myocardial microcirculation while minimizing bleeding risks makes it a superior anticoagulant choice for PCI in ACS patients, particularly the elderly, where balancing ischemic prevention and bleeding risk reduction is crucial for optimal clinical outcomes.

Balancing thrombotic risk and bleeding in elderly patients

Balancing thrombotic risk and bleeding complications in elderly patients undergoing PCI is challenging due to their elevated risks for both ACS and bleeding events. Bivalirudin has emerged as a favorable option, offering improved safety and efficacy. Zhang *et al*[3] showed that bivalirudin significantly reduces major bleeding incidents compared to unfractionated heparin while effectively managing thrombotic risks during PCI. Its direct thrombin inhibition prevents clot formation without causing widespread platelet activation. Du *et al*[1] highlighted that bivalirudin significantly enhances myocardial microcirculation, crucial for preventing complications like stent thrombosis and reinfarction in elderly patients with complex comorbidities. By promoting better blood flow, bivalirudin mitigates thrombotic risks while addressing bleeding tendencies. Recent findings from Natsuaki *et al*[6] suggest the potential for aspirin-free strategies in ACS management, particularly relevant for elderly patients at increased risk of gastrointestinal bleeding from prolonged aspirin use. Supporting bivalirudin's efficacy, Al-Abdoun *et al*[5] reported reduced net adverse clinical events in elderly PCI patients, consistent with Li *et al*[7], who noted lower rates of major adverse cardiac and cerebral events in elderly Chinese patients treated with bivalirudin compared to heparin. Briefly, choosing bivalirudin for anticoagulation in elderly PCI patients strategically balances thrombotic risk and bleeding concerns. Evidence supports bivalirudin's safety and effectiveness in high-risk populations, underscoring its role as a therapeutic option that enhances outcomes while minimizing complications associated with anticoagulation therapy.

Integrating modern antiplatelet strategies with bivalirudin

Integrating modern antiplatelet strategies with bivalirudin is crucial for optimizing outcomes in PCI patients. The landscape of antiplatelet therapy has evolved toward personalized approaches that minimize thrombotic events and mitigate bleeding risks. Bivalirudin, a direct thrombin inhibitor, has shown considerable safety advantages in PCI, especially for ACS patients. Zhang *et al*[3] found that bivalirudin significantly reduces major bleeding compared to traditional heparin, without sacrificing thrombotic protection. This benefit is particularly valuable for elderly patients or those with high bleeding risk. Recent studies, including the STOPDAPT-3 trial, have investigated alternative antiplatelet regimens, such as aspirin-free strategies[6]. These findings suggest that a tailored approach can achieve adequate platelet inhibition while reducing bleeding risks from long-term aspirin use. Incorporating bivalirudin into these strategies enables a balanced approach, where bivalirudin's immediate antithrombotic effects complement the sustained platelet inhibition of modern antiplatelet agents. Bivalirudin's ability to enhance myocardial microcirculation, as demonstrated by Du *et al*[1], underscores its role in antiplatelet therapy. Improved blood flow aids in preventing stent thrombosis and supports myocardial recovery in ACS settings. When combined with contemporary antiplatelet agents, bivalirudin contributes to a comprehensive strategy addressing both thrombotic and bleeding risks in PCI. Al-Abdoun *et al*[5] support the safe use of direct oral anticoagulants alongside antiplatelet therapy in post-ACS management, highlighting the potential synergy between bivalirudin and emerging antiplatelet agents to optimize outcomes. Integrating bivalirudin with modern antiplatelet strategies holds promise for enhancing patient outcomes during PCI. By leveraging

bivalirudin's safety and efficacy alongside contemporary antiplatelet therapies, clinicians can better manage thrombotic risk and bleeding, especially in high-risk populations such as the elderly. This multifaceted approach reflects current best practices and paves the way for future advancements in cardiovascular medicine.

Long-term safety and efficacy of bivalirudin

The long-term safety and efficacy of bivalirudin in patients undergoing PCI are central to cardiovascular research. As a direct thrombin inhibitor, bivalirudin may reduce thrombotic events and bleeding complications, particularly in ACS patients. Zhang *et al*[3] demonstrated that bivalirudin significantly lowers the risk of major bleeding compared to heparin without compromising clinical outcomes. This benefit is especially relevant for high-risk groups, such as elderly patients or those with complex medical histories. Long-term follow-up data from studies, including Omerovic *et al*[8], indicate that bivalirudin contributes to favorable outcomes regarding major adverse cardiac events over extended post-PCI periods. These findings align with results from the BRIGHT-4 trial, confirming the sustained safety of bivalirudin in both STEMI and non-STEMI patients, even two years after the procedure[2,6]. Bivalirudin's efficacy also extends to enhancing myocardial microcirculation. Research by Du *et al*[1] highlights that bivalirudin improves microvascular perfusion, essential for myocardial recovery and better long-term cardiac function. This is particularly beneficial for older patients, often more vulnerable to complications from both thrombotic and bleeding events. Integrating bivalirudin with modern antiplatelet strategies has shown promise in emerging treatment approaches, including aspirin-free regimens. Natsuaki *et al*[6] noted that bivalirudin can be used effectively with alternative antiplatelet therapies in high-bleeding-risk populations, potentially leading to better outcomes with fewer adverse effects. Furthermore, Al-Abdoun *et al*[5] observed a growing interest in combining direct oral anticoagulants with antiplatelet therapies for post-ACS management. Incorporating bivalirudin into such regimens may enhance patient safety and treatment efficacy. Shortly, the long-term safety and efficacy of bivalirudin underscore its value in managing patients undergoing PCI. Its unique properties provide effective anticoagulation while reducing bleeding risks, making it particularly advantageous for vulnerable populations. Continued research and clinical trials will help define optimal strategies for using bivalirudin in conjunction with evolving antiplatelet therapies, advancing outcomes in cardiovascular care.

Implications for clinical practice

Integrating bivalirudin into clinical practice for PCI patients offers significant opportunities to enhance patient safety and outcomes, particularly in managing ACS. Recent evidence supports bivalirudin's advantages over unfractionated heparin, mainly due to its favorable bleeding risk profile. Zhang *et al*[3] demonstrated bivalirudin's effectiveness in minimizing major bleeding events, benefiting high-risk populations, including the elderly. Findings from the BRIGHT-4 trial further support bivalirudin's use in both STEMI and non-STEMI populations, showing favorable outcomes for major adverse cardiac events[2]. These studies suggest that bivalirudin is an effective and versatile anticoagulant, reinforcing its role as a preferred choice in PCI settings where reducing bleeding risk is essential. Clinicians should consider bivalirudin for patients who could benefit from a lower bleeding risk without sacrificing efficacy. Its positive effects on myocardial microcirculation, particularly in older patients, underscore its potential to enhance cardiac recovery post-intervention, as demonstrated by Du *et al*[1]. Furthermore, shifts toward personalized antiplatelet therapy, such as the aspirin-free regimens explored by Natsuaki *et al*[6], highlight the importance of evaluating anticoagulation choices alongside evolving antiplatelet strategies. Bivalirudin's compatibility with innovative antiplatelet approaches enables a more customized anticoagulation strategy that enhances efficacy while minimizing adverse effects. In addition, the emerging practice of combining direct oral anticoagulants with antiplatelet therapies, as noted by Al-Abdoun *et al*[5], reflects an evolving paradigm in post-ACS management, where incorporating bivalirudin may further optimize patient outcomes and safety. Ultimately, bivalirudin is a compelling option for clinicians managing PCI patients, particularly those with ACS. Its unique safety profile, efficacy in reducing bleeding complications, and potential to support myocardial recovery make it a pivotal agent in cardiovascular care. Ongoing research and clinical experience will continue to refine its role, enabling more personalized and effective management strategies for patients at risk of thrombotic events. As understanding of bivalirudin's clinical applications evolves, healthcare providers should adapt protocols to maximize its benefits while ensuring patient-centered care.

Conclusion

The study by Du *et al*[1] provides promising preliminary insights into the use of bivalirudin in elderly ACS patients undergoing PCI. The findings suggest that bivalirudin may enhance myocardial microcirculation and procedural efficiency while reducing bleeding complications and adverse cardiac events. These benefits are particularly relevant for elderly patients, who face higher risks of ischemic and hemorrhagic complications due to age and comorbidities[4]. However, these results should be interpreted cautiously, given the study's limitations, including its retrospective design and potentially shorter procedure times. Further research is essential to confirm these findings and comprehensively evaluate the safety and efficacy of bivalirudin compared to heparin in this population[1]. Large-scale, multicenter clinical trials will be crucial for establishing standardized guidelines for bivalirudin use in elderly ACS patients. Future studies should also examine long-term outcomes associated with bivalirudin, including survival, quality of life, and healthcare costs related to PCI complications[4]. Addressing the clinical challenges posed by patient variability and comorbidities will be key in refining anticoagulation strategies and optimizing outcomes.

FOOTNOTES

Author contributions: Cheng CY and Hao WR jointly drafted the article, with both authors contributing to the formulation of key insights and perspectives; Cheng TH provided comprehensive revisions, adding depth and ensuring the article's relevance to clinical practice; and all authors collaborated in reviewing and refining the content, approving the final version for publication and endorsing its submission.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

Open Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <https://creativecommons.org/licenses/by-nc/4.0/>

Country of origin: Taiwan

ORCID number: Tzu-Hung Cheng 0000-0002-9155-4169.

S-Editor: Wei YF

L-Editor: A

P-Editor: Zhang YL

REFERENCES

- 1 Du YK, Cui LJ, Gao HB. Effect of bivalirudin on myocardial microcirculation and adverse events after interventional therapy in older patients with acute coronary syndrome. *World J Clin Cases* 2024; **12**: 4890-4896 [PMID: 39109044 DOI: 10.12998/wjcc.v12.i22.4890]
- 2 Stone GW, Valgimigli M, Erlinge D, Han Y, Steg PG, Stables RH, Frigoli E, James SK, Li Y, Goldstein P, Mehran R, Mehdiipoor G, Crowley A, Chen S, Redfors B, Snyder C, Zhou Z, Bickdeli B. Bivalirudin vs Heparin Anticoagulation in STEMI: Confirmation of the BRIGHT-4 Results. *J Am Coll Cardiol* 2024; **84**: 1512-1524 [PMID: 39384262 DOI: 10.1016/j.jacc.2024.07.045]
- 3 Zhang J, Chen Z, Wang D, Li C, Luo F, He Y. Bivalirudin versus heparin in contemporary percutaneous coronary interventions for patients with acute coronary syndrome: a systematic review and meta-analysis. *Cardiol J* 2024; **31**: 309-320 [PMID: 37964648 DOI: 10.5603/cj.90956]
- 4 Galli M, Bernardi M, Ortega-Paz L, Nerla R, D'Amario D, Franchi F, Biondi-Zoccai G, Angiolillo DJ. Bivalirudin in acute coronary syndromes. *Expert Rev Cardiovasc Ther* 2023; **21**: 901-911 [PMID: 37919937 DOI: 10.1080/14779072.2023.2273902]
- 5 Al-Abdoun A, Mhanna M, Jabri A, Madanat L, Alhuneafat L, Mostafa MR, Kundu A, Gupta V. Bivalirudin versus unfractionated heparin in patients with myocardial infarction undergoing percutaneous coronary intervention: A systematic review and meta-analysis of randomized controlled trials. *Cardiovasc Revasc Med* 2024; **61**: 52-61 [PMID: 37872022 DOI: 10.1016/j.carrev.2023.10.014]
- 6 Natsuaki M, Watanabe H, Morimoto T, Yamamoto K, Obayashi Y, Nishikawa R, Ando K, Domei T, Suwa S, Ogita M, Isawa T, Takenaka H, Yamamoto T, Ishikawa T, Hisauchi I, Wakabayashi K, Onishi Y, Hibi K, Kawai K, Yoshida R, Suzuki H, Nakazawa G, Kusuyama T, Morishima I, Ono K, Kimura T. An Aspirin-Free Versus Dual Antiplatelet Strategy for Coronary Stenting: STOPDAPT-3 Randomized Trial. *Circulation* 2024; **149**: 585-600 [PMID: 37994553 DOI: 10.1161/CIRCULATIONAHA.123.066720]
- 7 Li Q, Li H, Liu Z, Duan L. Bivalirudin versus Heparin on Net Adverse Clinical Events, Major Adverse Cardiac and Cerebral Events, and Bleeding in Elderly Chinese Patients Treated with Percutaneous Coronary Intervention. *Tohoku J Exp Med* 2024; **262**: 115-124 [PMID: 37821386 DOI: 10.1620/tjem.2023.J085]
- 8 Omerovic E, James S, Råmundal T, Fröbert O, Linder R, Danielewicz M, Hamid M, Pagonis C, Henareh L, Wagner H, Stewart J, Jensen J, Lindros P, Robertsson L, Wikström H, Ulvenstam A, Bhiladval P, Tödt T, Ioanes D, Kellerth T, Zagozdzon L, Götzberg M, Andersson J, Ångerås O, Östlund O, Held C, Koul S, Erlinge D. Bivalirudin versus heparin in ST and non-ST-segment elevation myocardial infarction- Outcomes at two years. *Cardiovasc Revasc Med* 2024; **66**: 43-50 [PMID: 38575449 DOI: 10.1016/j.carrev.2024.03.025]



Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

Telephone: +1-925-3991568

E-mail: office@baishideng.com

Help Desk: <https://www.f6publishing.com/helpdesk>

<https://www.wjgnet.com>

