https://doi.org/10.36290/vnl.2025.087

Drug-Drug interaction between rivaroxaban and amiodarone: A systematic review

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Background: The concurrent use of rivaroxaban and amiodarone in cardiovascular patients raises concerns about potential drug-drug interactions and increased bleeding risk. Objective: This systematic review aimed to evaluate the impact of combining amiodarone with rivaroxaban on bleeding events compared to rivaroxaban monotherapy in cardiovascular patients. Methods: We systematically reviewed observational studies and clinical trials examining bleeding outcomes in patients receiving rivaroxaban with or without concurrent amiodarone therapy. Studies were included if they reported clinical bleeding outcomes, included both combination therapy and monotherapy groups, and provided comparative statistical analyses. Results: Eight studies comprising over 130.000 patients were analyzed. The combination of rivaroxaban and amiodarone was associated with significantly increased bleeding risk across multiple studies, with hazard ratios ranging from 1.10 to 2.83. The risk difference ranged from 13.94 to 29.7 events per 1000 person-years, with higher risks observed in patients with elevated HAS-BLED scores and renal impairment. Major bleeding events were consistently elevated, although often without reaching statistical significance, and the interaction appeared specific to amiodarone compared to other antiarrhythmic drugs. Pharmacokinetic studies demonstrated increased rivaroxaban plasma concentrations when co-administered with amiodarone, particularly at higher doses and in patients with renal dysfunction. Conclusions: The combination of rivaroxaban and amiodarone significantly increases bleeding risk compared to rivaroxaban monotherapy, necessitating careful risk-benefit assessment and enhanced monitoring in patients requiring both medications.

Key words: rivaroxaban, amiodarone, drug interactions, P-glycoprotein, CYP3A4, bleeding risk.

Léková interakce mezi rivaroxabanem a amiodaronem: systematický přehled

Úvod: Súčasné používanie rivaroxabanu a amiodarónu u kardiovaskulárnych pacientov vyvoláva obavy z potenciálnych liekových interakcií a zvýšeného rizika krvácania. Cieľ: Tento systematický prehľad mal za cieľ vyhodnotiť vplyv kombinácie amiodarónu s rivaroxabanom na výskyt krvácania v porovnaní s monoterapiou rivaroxabanom u kardiovaskulárnych pacientov. Metódy: Systematicky sme preskúmali observačné štúdie a klinické skúšania skúmajúce výskyt krvácania u pacientov užívajúcich rivaroxaban so súčasnou terapiou amiodarónom alebo bez nej. Štúdie boli zahrnuté, ak uvádzali klinické výsledky krvácania, zahŕňali skupiny s kombinovanou terapiou aj monoterapiou a poskytovali porovnávacie štatistické analýzy. Výsledky: Analyzovaných bolo osem štúdií zahŕňajúcich viac ako 130 000 pacientov. Kombinácia rivaroxabanu a amiodarónu bola spojená s významne zvýšeným rizikom krvácania vo viacerých štúdiách, s pomermi rizika (hazard ratio) v rozmedzí od 1,10 do 2,83. Rozdiel rizika sa pohyboval od 13,94 do 29,7 udalostí na 1000 osoborokov, pričom vyššie riziká boli pozorované u pacientov so zvýšeným HAS-BLED skóre a poruchou funkcie obličiek. Závažné krvácavé príhody boli konzistentne zvýšené, hoci často štatisticky nevýznamne, a interakcia sa javila ako špecifická pre amiodarón v porovnaní s inými antiarytmikami. Farmakokinetické štúdie preukázali zvýšené plazmatické koncentrácie rivaroxabanu pri súčasnom podávaní s amiodarónom,

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Cit. zkr: Vnitř Lék. 2025;71(7):E1-E6
Článek přijat redakcí: 27. 8. 2025
Článek přijat po recenzích: 2. 10. 2025

najmä pri vyšších dávkach a u pacientov s renálnou dysfunkciou. Závery: Kombinácia rivaroxabanu a amiodarónu významne zvyšuje riziko krvácania v porovnaní s monoterapiou rivaroxabanom, čo si vyžaduje dôkladné posúdenie pomeru rizika a prínosu a zvýšené monitorovanie u pacientov vyžadujúcich obidva lieky.

Kľúčové slová: rivaroxaban, amiodarón, liekové interakcie, P-glykoproteín, CYP3A4, riziko krvácania.

Introduction

Direct oral anticoagulants have revolutionized the management of atrial fibrillation and venous thromboembolism, offering predictable pharmacokinetics without routine monitoring requirements. Rivaroxaban, a direct factor Xa inhibitor, is widely prescribed for stroke prevention in atrial fibrillation and treatment of thromboembolic disorders. However, despite its advantages over warfarin, rivaroxaban remains subject to drug-drug interactions through cytochrome P450 3A4 and P-glycoprotein pathways.

Amiodarone, a class III antiarrhythmic agent, remains a cornerstone therapy for rhythm control in atrial fibrillation and ventricular arrhythmias. As both a P-glycoprotein and moderate CYP3A4 inhibitor, amiodarone theoretically increases rivaroxaban exposure, potentially elevating bleeding risk. Given that many patients with atrial fibrillation require both anticoagulation and rhythm control, understanding this interaction has substantial clinical implications.

Previous studies have suggested variable effects of this drug combination, with some reporting significant bleeding increases while others found minimal impact. This systematic review synthesizes current evidence regarding the bleeding risk associated with concurrent rivaroxaban and amiodarone use compared to rivaroxaban monotherapy, aiming to provide clinicians with comprehensive risk assessment data.

Methods

Search Strategy and Study Selection

A systematic search was conducted across over 126 million academic papers from the Semantic Scholar corpus to identify studies examining the interaction between rivaroxaban and amiodarone. Studies were included if they met the following criteria: examination of patients using amiodarone and rivaroxaban concurrently, inclusion of a control group using rivaroxaban monotherapy, utilization of either randomized controlled trial or observational cohort design, and reporting of clinical outcomes beyond pharmacokinetic interactions alone.

Data Extraction and Quality Assessment

Data extraction focused on study design, patient population characteristics, comparison group characteristics, and primary outcome measures. For each study, we extracted bleeding event rates, risk ratios or hazard ratios with confidence intervals. Studies were categorized by design type, with assessment of follow-up duration and outcome definitions.

Statistical Analysis

Given the heterogeneity in study designs and outcome definitions, a narrative synthesis approach was employed. Bleeding outcomes were categorized as major bleeding, clinically relevant non-major bleeding, and minor bleeding according to International Society on Thrombosis and Haemostasis criteria where available (1).

Results

Study Characteristics

Eight studies meeting inclusion criteria were identified, encompassing 137,176 patients in rivaroxaban treatment arms (Table 1). Four studies employed retrospective cohort designs, while two utilized prospective observational approaches, one employed a nested case-control design within a retrospective cohort, and one analyzed post-hoc subgroup data from a randomized controlled trial (2-9). Study populations ranged from 174 to 54,006 participants, with follow-up durations varying from three months to four years. Most studies focused on patients with atrial fibrillation requiring anticoagulation, though specific inclusion criteria varied.

Tab. 1. *Characteristics of Included Studies*

Study	Study Design	Population Size	Follow-up Duration	Primary Outcomes
Ray et al., 2023 (2)	Retrospective cohort	91,590 (38,193 rivaroxaban)	Median 159 days (IQR 59-180)	Bleeding-related hospitalization
Wang et al., 2023 (3)	Prospective observational with propensity score matching	481	3 months	Composite bleeding events
Ding et al., 2024 (4)	Prospective cohort	174	≥4 weeks (180 days for outcomes)	Bleeding events, PK/PD measures
Chiou et al., 2020 (5)	Retrospective multicenter cohort	1,777	Mean 31–34 months	Safety, effectiveness, MACE
Chang et al., 2017 (6)	Retrospective cohort	91,330 (54,006 rivaroxaban)	4 years	Major bleeding
Gronich et al., 2021 (7)	Nested case-control	89,284 (10,305 rivaroxaban)	126,302 patient-years	Serious bleeding, stroke/SE
Wu et al., 2024 (8)	Retrospective cohort with propensity matching	78,805 (17,976 rivaroxaban)	2.56 ± 1.73 years	Major bleeding
Steinberg et al., 2014 (9)	Post-hoc RCT subgroup analysis	14,264	Median 20–21 months	Stroke, bleeding, death

Overall Bleeding Risk

The combination of rivaroxaban and amiodarone consistently demonstrated increased bleeding risk compared to rivaroxaban monotherapy across most studies (Table 2). Ray et al. reported bleeding-related hospitalization rates of 56.5 per 1000 person-years with combination therapy versus 39.0 per 1000 person-years with rivaroxaban plus alternative antiarrhythmics, yielding a hazard ratio of 1.44 (2). When comparing rivaroxaban plus amiodarone specifically to apixaban plus amiodarone, the bleeding rate increased to 78.2 versus 39.5 per 1000 person-years respectively, with a hazard ratio of 2.0.

Wang et al. found a substantially elevated bleeding risk at three months, with 29.1% of patients experiencing bleeding events on combination therapy versus 12.6% on rivaroxaban alone, corresponding to a hazard ratio of 2.76 (3). Similarly, Ding et al. reported bleeding events in 16.1% versus 6.3% of patients, with a hazard ratio of 2.83 (4).

Figure 1. provides a visual comparison of hazard ratios across studies, illustrating the consistent trend toward increased bleeding risk with combination therapy. The magnitude of effect varied from minimal (HR 1.06, Steinberg et al., 2014) to substantial (HR 2.83, Ding et al., 2024), with most studies demonstrating statistically significant increases.

Bleeding Categories

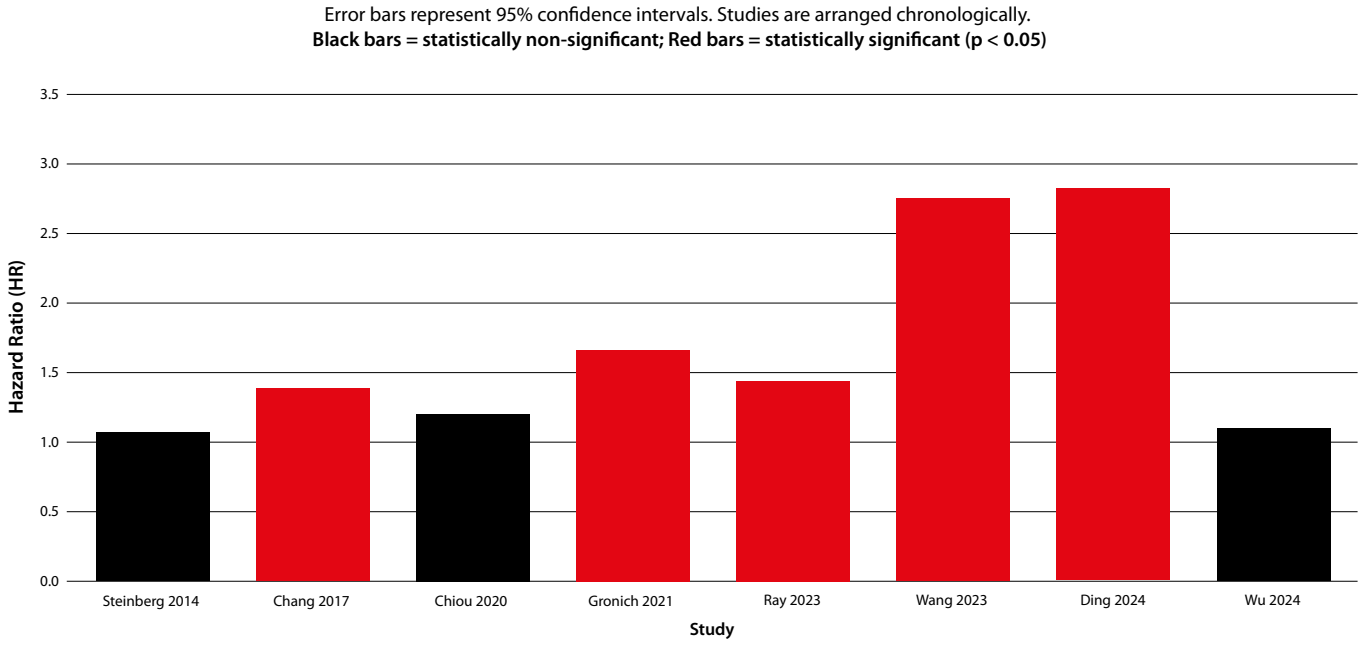
Analysis of bleeding severity revealed differential effects across bleeding categories (Table 3). Major bleeding events showed variable increases across studies, with Ray et al. reporting 1335 versus 404 hospitalizations with a hazard ratio of 1.44 for major bleeding (2). Wang et al. found no major bleeding events in the combination therapy group versus four in the monotherapy group, though this difference was not statistically significant (3).

Clinically relevant non-major bleeding demonstrated more consistent elevation with combination therapy. Ray et al. reported 1161

Tab. 2. *Overall Bleeding Risk*

Study	Treatment Comparison	Bleeding Event Rate	Risk Ratio (95% CI)
Ray et al., 2023 (2)	Rivaroxaban + amiodarone vs alternative AADs	56.5 vs 39.0 per 1000 PY	HR 1.44 (1.27-1.63)
	Rivaroxaban + amiodarone vs apixaban + amiodarone	78.2 vs 39.5 per 1,000 person-years	HR 2.0 (p = 0.0012)
Wang et al., 2023 (3)	Rivaroxaban + amiodarone vs rivaroxaban	29.1% vs 12.6% (3 months)	HR 2.76 (1.55-4.93)
Ding et al., 2024 (4)	Rivaroxaban + amiodarone vs rivaroxaban	16.1% vs 6.3% (180 days)	HR 2.83 (1.05-7.66), p = 0.041
Chiou et al., 2020 (5)	Rivaroxaban + amiodarone vs rivaroxaban	13% vs 10.8%	HR 1.2 (p=0.74)
Chang et al., 2017 (6)	Rivaroxaban + amiodarone vs rivaroxaban	52.78 vs 41.64 per 1000 PY	HR 1.38 (1.21-1.58), (p<0.01)
Gronich et al., 2021 (7)	Rivaroxaban + amiodarone vs rivaroxaban	8% vs 5.2%	OR 1.66 (1.12-2.46), (p=0.012)
Wu et al., 2024 (8)	Rivaroxaban + amiodarone vs rivaroxaban	2.23% vs 2.01%	HR 1.10 (0.98-1.25), (p=0,616)
Steinberg et al., 2014 (9)	Rivaroxaban + amiodarone vs rivaroxaban	15.9 vs 15.0 per 100 PY	HR 1.06 (0.94-1.92) (p=0.71)

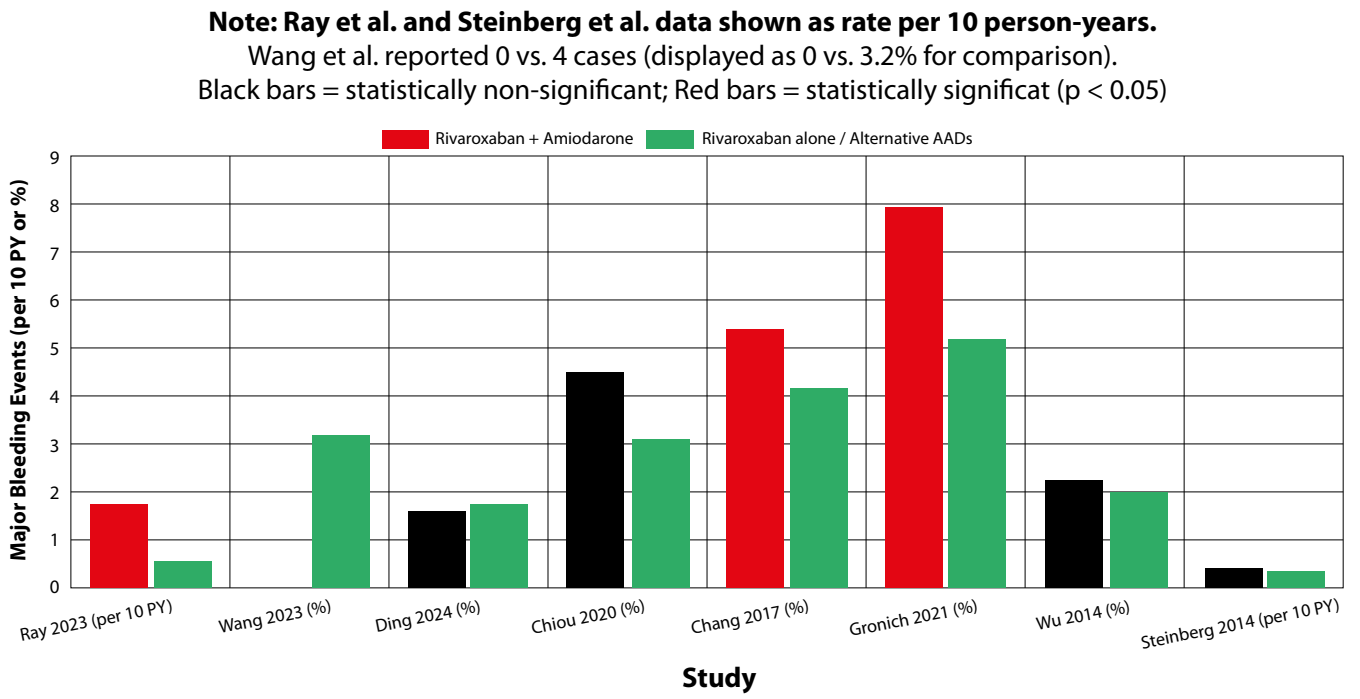
Fig. 1. *Hazard Ratios for Bleeding Risk with Rivaroxaban + Amiodarone vs Rivaroxaban*



Tab. 3. *Bleeding Categories*

Study	Major Bleeding	Clinically Relevant Non-Major Bleeding	Minor Bleeding
Ray et al., 2023 (2)	1335 vs 404 hospitalizations, HR 1.44 (1.27-1.63) rate/1000 PY; 174 pts vs 59 major bleeding HR 1.42 (1.02-1.96) rate/1000 PY, (p = 0.0012)	1161 vs 365, HR 1.44 (1.26-1.65) rate/1000 PY, (p = 0.0012)	Not reported
Wang et al., 2023 (3)	0 vs 4 (p=0.149)	31 vs 16 (p<0.001)	26 vs 16 (p=0.005)
Ding et al., 2024 (4)	1 (1.6%) vs 2 (1.79%) (P=0.928)	9 (14.5%) vs 5 (4.5%) (p=0.021), HR 3.65 (1.21–10.94)	Not reported
Chiou et al., 2020 (5)	8 (4.5%) vs 37 (3.1%) (p=0.74)	4 (2.3%) vs 48 (4.0%) (p=0.692)	19 (10.7%) vs 106 (8.8%), p=0.769
Chang et al., 2017 (6)	685 (5.4%) vs 1809 (4.16%) (p<0.01)	Not reported	Not reported
Gronich et al., 2021 (7)	35 (8%) vs 515 (5.2%) (p=0.012)	Not reported	Not reported
Wu et al., 2024 (8)	519 (2.23%) vs 531 (2.01%) (p=0,616)	Not reported	Not reported
Steinberg et al., 2014 (9)	29 (3.84 per 100 PY) vs 343 (3.61 per 100 PY) (p=0.71)	85 (12.28 per 100 PY) vs 1035 (11.92 per 100 PY) (p=0.71)	Not reported

Fig. 2. *Major Bleeding Events - Rivaroxaban + Amiodarone vs Rivaroxaban Monotherapy*



versus 365 events with a hazard ratio of 1.44, while Wang et al. found 31 versus 16 events, and Ding et al. reported 14.5% versus 4.5% incidence with a hazard ratio of 3.65 (2-4). Minor bleeding was reported in fewer studies but showed significant increases where measured, with Wang et al. reporting 26 versus 16 events and Chiou et al. finding 10.7% versus 8.8% incidence (3,5).

Figure 2 visualizes the impact of rivaroxaban-amiodarone combination on major bleeding events across all studies. Ray et al. demonstrated the highest absolute risk with 1.74 events per 10 person-years for combination therapy versus 0.59 for alternative antiarrhythmics (HR 1.42, p=0.0012) (2), representing nearly a three-fold increase. Note that Ray et al. and Steinberg et al. data represent rates per 10 person-years, while other studies report percentages (2, 9). Wang et al. found no major bleeding events in the combination group versus 4 cases in the monotherapy group, though this difference was not statistically significant (p=0.149) (11). Among studies reporting percentages, Gronich et al. showed the highest rate at 8.0% versus 5.2% (p=0.012) (7), while Chang et al. reported 5.4% versus 4.16% (p<0.01) (6). Steinberg et al. showed minimal difference with 0.384 versus 0.361 events per 10 person-years (p=0.71) (9). The variability in effect sizes across studies likely reflects differences in patient populations, follow-up duration, and bleeding definitions.

Patient-Specific Risk Factors

The interaction between rivaroxaban and amiodarone showed particular significance in specific patient populations. Ray et al. demonstrated that bleeding risk increased proportionally with HAS-BLED scores (2). The stratified analysis revealed distinct patterns based on bleeding risk assessment and anticoagulant choice (Figure 1).

In patients with HAS-BLED scores of 2 or lower, the rate difference for rivaroxaban plus amiodarone was 24.1 events per 1000 person-years compared to only 1.2 events for apixaban plus amiodarone. For HAS-BLED scores greater than 2, rate differences increased to 29.7 events per 1000 person-years for rivaroxaban versus 13.3 events for apixaban when combined with amiodarone. The absolute bleeding rates with rivaroxaban plus amiodarone reached 120.8 per 1000 person-years in

Tab. 4. *Risk for Bleeding-Related Hospitalizations with Adding Amiodarone to Apixaban or Rivaroxaban in Patients with Atrial Fibrillation (2)*

HAS-BLED Score	Anticoagulant	Amiodarone Group	Flecainide/Sotalol Group	Rate Difference (95% CI)
		Events/PY (Rate per 1000 PY)	Events/PY (Rate per 1000 PY)	Per 1000 PY
HAS-BLED ≤2				
	Apixaban	78/3051 (25.6)	45/3071 (14.7)	1.2 (-6.5 to 8.9)
	Rivaroxaban	144/2369 (60.8)	63/2536 (24.8)	24.1 (12.0 to 36.2)
HAS-BLED >2				
	Apixaban	501/7758 (64.6)	128/4194 (30.5)	13.3 (4.5 to 22.0)
	Rivaroxaban	612/5067 (120.8)	168/3120 (53.8)	29.7 (16.0 to 43.4)

PY = person-years; CI = confidence interval. Adjusted incidence with overlap weighting.

high-risk patients compared to 60.8 per 1000 person-years in low-risk patients.

Renal function emerged as a critical modifier of bleeding risk. Ding et al. found that amiodarone significantly increased rivaroxaban trough plasma concentrations, particularly in patients receiving 20 mg doses and those with moderate to severe renal impairment (4). This pharmacokinetic interaction likely explains the clinical bleeding observations, as reduced renal clearance compounds the inhibitory effect of amiodarone on rivaroxaban metabolism.

Comparative Safety with Other Antiarrhythmic Drugs

The bleeding risk appeared specific to amiodarone among antiarrhythmic drugs. Ray et al. found no significant bleeding increase with flecainide or sotalol combined with rivaroxaban (2). Chang et al. similarly reported no elevated risk with dronedarone (6). This specificity suggests that the interaction relates to amiodarone's particular pharmacokinetic properties rather than a class effect of antiarrhythmic agents.

Discussion

This systematic review demonstrates that combining amiodarone with rivaroxaban significantly increases bleeding risk compared to rivaroxaban monotherapy, with most studies showing statistically significant elevations in bleeding events. The magnitude of risk increase varied considerably across studies, likely reflecting differences in patient populations, follow-up duration, and outcome definitions.

The interaction between amiodarone and rivaroxaban occurs through inhibition of two closely linked systems: the CYP3A4 enzyme and P-glycoprotein transporter. These two systems work together as a functional unit in the intestine, liver, and kidneys to limit drug absorption and enhance elimination. They share the same regulatory mechanisms and typically have the same substrates, inhibitors, and inducers. When amiodarone inhibits both systems simultaneously, it disrupts rivaroxaban elimination at multiple sites (10,11).

In the intestinal wall, P-glycoprotein and CYP3A4 create a coordinated barrier. P-glycoprotein pumps absorbed rivaroxaban back into the gut lumen while CYP3A4 metabolizes it within intestinal cells. Importantly, CYP3A4 oxidation can modify rivaroxaban to increase its affinity for P-glycoprotein transport, enhancing the efficiency of this elimination system. When amiodarone blocks both processes, this synergistic mechanism is disrupted, allowing more unchanged rivaroxaban to reach the bloodstream. The same dual inhibition occurs in the liver (reducing metabolism) and kidneys (reducing active secretion). Because these systems cooperate through this substrate modification mechanism rather than working independently, their simultaneous inhibition by amiodarone produces a greater effect than would occur from blocking either system alone (10,12).

This combined inhibition significantly increases rivaroxaban blood levels, with studies showing 36-100% increases in total drug exposure (AUC) and 40-61% increases in peak concentrations (Cmax) (11,12,13). Kaserer et al. found nearly twice the risk of excessive rivaroxaban levels (>50 mcg/L) in patients with kidney problems taking amiodarone (12). Lin et al. reported that 16.4% of patients on amiodarone had dangerously high drug levels versus 9.4% in controls (13). The interaction is most pronounced in patients with renal impairment, where the CYP3A4/P-glycoprotein system becomes even more important for drug elimination (11).

A unique characteristic of this interaction is its persistence after amiodarone discontinuation. Given amiodarone's long elimination half-life (up to several weeks) and its extensive tissue distribution, supratherapeutic rivaroxaban concentrations can persist for weeks after stopping amiodarone (14). This has significant implications for clinical management of patients. Ding et al. provided direct evidence of this mechanism, demonstrating elevated rivaroxaban trough levels with concurrent amiodarone use (4). This effect was particularly pronounced in patients with renal impairment, where reduced clearance compounds the interaction.

The clinical implications of these findings are substantial. Clinicians must carefully weigh the benefits of rhythm control with amiodarone against increased bleeding risk when patients require rivaroxaban anticoagulation. The risk appears highest in patients with elevated HAS-BLED scores and renal dysfunction, suggesting these patients require particularly careful monitoring or consideration of alternative therapies.

Alternative antiarrhythmic agents such as dronedarone, flecainide, or sotalol may offer safer options for patients requiring both anticoagulation and rhythm control. The absence of significant bleeding increases with these agents suggests they could be preferentially considered when clinically appropriate. However, amiodarone's superior efficacy for rhythm control in certain clinical scenarios may necessitate accepting increased bleeding risk with appropriate monitoring.

Several limitations warrant consideration. First, most included studies were observational, introducing potential for residual confounding despite statistical adjustments. Second, bleeding definitions varied across studies, complicating direct comparisons. Third, the duration of follow-up differed substantially, potentially affecting observed event

rates. Fourth, dose-specific analyses were limited, preventing detailed assessment of dose-response relationships.

Future research should focus on prospective evaluation of risk mitigation strategies, including dose adjustment algorithms based on renal function and clinical risk scores. Additionally, investigation of monitoring strategies, such as rivaroxaban level measurement in high-risk patients, could inform individualized management approaches.

Conclusions

The combination of rivaroxaban and amiodarone is associated with significantly increased bleeding risk compared to rivaroxaban monotherapy, with risk elevations ranging from modest to substantial across different patient populations. This interaction appears mediated by pharmacokinetic mechanisms, with particular impact in patients with renal impairment or high baseline bleeding risk. When both medications are clinically necessary, enhanced monitoring and consideration of dose adjustment may be warranted. Alternative antiarrhythmic agents should be considered when appropriate, as they appear to carry lower interaction potential. These findings underscore the importance of individualized risk-benefit assessment when managing patients requiring both anticoagulation and antiarrhythmic therapy.

PROHLÁŠENÍ AUTORŮ: **Prohlášení o původnosti:** Publikace byla zpracována s využitím uvedené literatury a nebyla publikována ani zaslána k recenznímu řízení do jiného média. **Střet zájmů:** Žádný. **Financování:** Ne. **Poděkování:** N/A. **Registrace v databázích:** N/A. **Projednání etickou komisí:** N/A.

REFERENCES

1. Schulman S, Kearon C; Subcommittee on Control of Anticoagulation of the Scientific and Standardization Committee of the International Society on Thrombosis and Haemostasis. Definition of major bleeding in clinical investigations of antihemostatic medicinal products in non-surgical patients. J Thromb Haemost 2005; 3(4): 692-694.
2. Ray WA, Chung CP, Stein M et al. Risk for bleeding-related hospitalizations during use of amiodarone with apixaban or rivaroxaban in patients with atrial fibrillation: A retrospective cohort study. Ann Intern Med 2023; 176(6): 769-778.
3. Lv Q, Wang Z, Li X et al. Combination of rivaroxaban and amiodarone increases bleeding in patients with atrial fibrillation. Ann Pharmacother 2023; 57(8): 891-899.
4. Nishida K, Davies NM, Ding H et al. Co-administration of amiodarone increases bleeding by affecting rivaroxaban pharmacokinetics in patients with atrial fibrillation. Pharmaceutics 2024; 16(3): 421.
5. Chiou WR, Huang CC, Lin PL et al. Safety and effectiveness of rivaroxaban in combination with various antiarrhythmic drugs in patients with non-permanent atrial fibrillation. Am J Cardiovasc Drugs 2020; 21(4): 459-469.
6. Chang SH, Chou IJ, Yeh YH et al. Association between use of non-vitamin K oral anticoagulants with and without concurrent medications and risk of major bleeding in nonvalvular atrial fibrillation. JAMA 2017; 318(13): 1250-1259.
7. Gronich N, Stein N, Muszkat M. Association between use of pharmacokinetic-interacting drugs and effectiveness and safety of direct acting oral anticoagulants: Nested case--control study. Clin Pharmacol Ther 2021; 110(6): 1526-1536.
8. Chien V, Wu HC, Wang CL et al. Bleeding associated with antiarrhythmic drugs in patients with atrial fibrillation using direct oral anticoagulants: A nationwide population cohort study. J Am Heart Assoc 2024; 13(2): e029652.
9. Steinberg BA, Hellkamp AS, Lokhnygina Y et al. Use and outcomes of antiarrhythmic therapy in patients with atrial fibrillation receiving oral anticoagulation: Results from the ROCKET AF trial. Heart Rhythm 2014; 11(6): 925-932.
10. Grymonprez M, Carnoy L, Capiau A et al. Impact of P-glycoprotein and CYP3A4-interacting drugs on clinical outcomes in patients with atrial fibrillation using non-vitamin K antagonist oral anticoagulants. Eur Heart J Cardiovasc Pharmacother 2023; 9(8): 722-730.
11. Wang Z, Cheong EJY, Kojodjojo P et al. Model-based risk prediction of rivaroxaban with amiodarone for moderate renal impaired elderly population. Cardiovasc Drugs Ther 2023; 37(3): 605-609.
12. Kaserer A, Schedler A, Jetter A et al. Risk factors for higher-than-expected residual rivaroxaban plasma concentrations in real-life patients. Thromb Haemost 2018; 118(5): 808-817.
13. Lin SY, Liu YB, Ho LT et al. Impact of amiodarone on plasma concentration of direct oral anticoagulant in patients with atrial fibrillation. J Formos Med Assoc 2023; 122(8): 776-784.
14. Skov K, Falskov B, Jensen EA et al. Supratherapeutic rivaroxaban levels: A persistent drug-drug interaction after discontinuation of amiodarone. Basic Clin Pharmacol Toxicol 2020; 127(4): 351-353.