Effectiveness of Tirofiban in Patients Undergoing Percutaneous Coronary Intervention for ST-Segment Elevation Myocardial Infarction: A Meta-Analysis of Randomized Clinical Trials

Zia ur Rahman [a]	Irfan Ali Khan [b]	Qazi Najeeb Ullah Amin [c]
Kashif Ullah [d]	Farman Ullah [e]	Sami Ullah [f]

Abstract: Whether or whether or not tirofiban is beneficial within side the quick time period for sufferers with STEMI who go through PCI is debatable. A meta-analysis validated the short-term efficacy and safety of tirofiban in patients with ST-phase elevation myocardial infarction (STEMI) undergoing percutaneous coronary intervention (PCI). Comparing STEMI patients undergoing PCI with and without tirofiban. We found all relevant randomised controlled trials by searching scientific databases and websites. This fixed-results model computed RR and 95% CI. 10 RCTs included 5008 people. After 30 days, death from any cause (RR 0.79, CI 0.55-1.12, P=0.18), major bleeding (1.37, 0.93-2.03, P=0.11), or transfusion (1.23, 0.94-1.61, P=0.13) were no longer impacted. Minor bleeding (1.29, 1.02-1.63, P=0.04), thrombocytopenia (2.04, 1.40-2.97, P=0.0002), and 6-month all-purpose mortality (0.57, 0.36-0.90, P=0.02) showed statistically significant differences. Repeat revascularization (0.58, 0.43-0.78, P=0.0004) and myocardial infarction (0.55, 0.33-0.92, P=0.02) also differed. Mild bleeding and thrombocytopenia are more common with tirofiban, although reinfarction, revascularization, and death after 6 months are decreased.

Key Words: Tirofiban, Percutaneous Coronary Intervention, ST-Segment Elevation, Myocardial Infarction

Introduction

Tirofiban is a GP IIb/IIIa inhibitor (GPI) that reduces thrombus formation by blocking the binding of fibrinogen, von Willebrand factor, and other ligands to IIb/IIIa receptors. Tirofiban's ability to lessen platelet clumping is a significant benefit. Patients with NSTEMI and STEMI in the 2000s often used this medication as an antiplatelet prior to undergoing percutaneous coronary intervention (PCI), which is a kind of heart surgery. Although tirofiban's place in medical effects is still up in the air, it has been shown to bind to the vitronectin receptor and may have anti-inflammatory characteristics that are independent of GP IIb/IIIa. The antiaggregating consequences of tirofiban had been proven in each animal research and early human trials (Bai, N., Niu, Y.,

[a] MBBS, FCPS, Department of Cardiology, Hayatabad Medical Complex, Peshawar, KP, Pakistan.
[b] MBBS, FCPS, Department of Cardiology, Hayatabad Medical Complex, Peshawar, KP, Pakistan.
[c] MBBS, FCPS, Department of Cardiology, Hayatabad Medical Complex, Peshawar, KP, Pakistan.
  Email: qazinajeeb123yahoo.com *(Corresponding Author)*
[d] MBBS, FCPS, Department of Cardiology, Hayatabad Medical Complex, Peshawar, KP, Pakistan.
[e] MBBS, FCPS, Department of Cardiology, Hayatabad Medical Complex, Peshawar, KP, Pakistan.
[f] MBBS, FCPS, Department of Cardiology, Hayatabad Medical Complex, Peshawar, KP, Pakistan.

Ma, Y., et. al 2022; Allencherril, J., Alam, M., Levine, et. al 2018). Subsequently, some of research have been done to examine whether or not or now no longer tirofiban stepped forward consequences for PCI sufferers. Multiple take a look at findings have proven that tirofiban may also have long-time period healing benefits in lowering composite ischemic endpoints, including mortality (Fagel, N. D. 2022; Wang, J. (n.d). Long-time period tracking is described as 8 to 11 years after remedy ends, while short-time period tracking is described as one year. Tifosiban`s efficacy withinside the 30-day and six-month post-PCI follow-up duration for sufferers with STEMI is, however, nonetheless up for debate. Trioseparin, or tirofiban, turned into proven to appreciably lessen the primary final results at 30 days and six months throughout meta-analyses [8-10]. Another takes a look at said a large discount in important consequences at 30 days however now no longer at 6 months, such as all-motive mortality, myocardial infarction (MI), and pressing revascularization (Kingma, J. G. 2018; Verdoia, M., Kedhi, E., 2019). Lack of medical impact from tirofiban remedy has been proven in research lasting 30 days or 6 months Tsujimoto, Y., Fujii, T., et. al 2020; Tavenier, A. H., Hermanides, R. S., et. al 2019). The findings of trials 17 and 18 propose that thienopyridines and fibrinolysis may also lessen the short-time period effectiveness of tirofiban. Obviously, we want greater facts in this subject.

A meta-evaluation turned into finished to confirm the short-time period effectiveness and protection of tirofiban in sufferers with STEMI present process PCI. The effects confirmed that sufferers with STEMI may also have short-time period benefits with tirofiban regardless of the accelerated chance of bleeding and thrombocytopenia, and that damaging consequences of the drug may be reduced through deciding on thienopyridines.

Material and Methods

Different sources had been analysed among February 1 and July 31 of this yr. Studies had been constrained to randomised managed trials that evaluated the efficacy and protection of tirofiban in sufferers with STEMI after percutaneous coronary intervention. The following seek terms had been used: tiagabine, ST-elevation myocardial infarction, and placebo-managed trial (Supplementary Table 1). There had been no constraints on both the language or the term wherein the book can be published. An alert machine became created in order that human beings may want to maintain up with the maximum present-day research. Trials evaluating sufferers dealt with tirofiban to people who had been now no longer had been covered, as had been the ones reporting danger of mortality at 30 days or 6 months following a clinically described ST-elevation myocardial infarction (STEMI) with continual myocardial ischemia signs and electrocardiographic proof however without angiographic choice standards. This evaluation did now no longer encompass any research that had been now no longer randomised managed trials or the ones had individuals who did now no longer have ST-elevation myocardial infarction. Primary efficacy results had been 30- and 6-month dying from any cause, repeat MI, revascularization, and very last thrombolysis in myocardial infarction (TIMI) float grade 3. Bleeding of various stages of severity, thrombocytopenia, and the want for transfusions had been all foremost unfavorable effects. The covered medical trials described standards for categorising bleeding intensity, thrombocytopenia status, and the requirement for a blood transfusion.

Results

Search Results and Study Characteristics

An overall of 799 highlighted items had been culled from numerous on-line retailers. After looking via way of means of name and abstract, 18 articles had been discovered (Figure 1). Ten randomised managed trials (RCTs) encompassing 5008 sufferers with STEMI and PCI had been discovered after an intensive evaluation of the entire text. Of them, 2518 had been assigned to acquire tirofiban and 2490 had been assigned to acquire a placebo. In this study, simplest human

beings above the age of 18 took part. The common age of this study`s individuals became 61.06 years. In addition, 75.04% had been males, 52.77 % had been hypertensive, and 17.15% had been diabetic. Patients with dyslipidemia (such as hyperlipidemia and hypercholesterolemia) made up a giant minority, accounting for 42. seventy one percent. Acute myocardial infarction became recognized among 6- and 48-hours following symptom onset, and sufferers who met those standards had been covered withinside the study. Patients withinside the tirofiban organization were given the drug as a bolus dose of 25 mcg/kg, accompanied via way of means of an infusion over the direction of 18 hours at a charge of 0.15 g/kg/min (Bentur, O. S., Li, J.,

Jiang, C. S., 2021). Despite the reality that each one trials used unfractionated heparin and aspirin, they did now no longer all utilize the medicines withinside the equal way or on the equal amounts. Treatment with clopidogrel became favored. The covered research covered a one-year follow-up period, starting from in-sanatorium care via post-discharge monitoring. The demographic and medical history of the sufferers is laid forth. Treatment with percutaneous transluminal coronary angioplasty or coronary artery skip grafting withinside the beyond is what is supposed via way of means of "preceding revascularization." Multivessel lesions arise while there may be stenosis or occlusion in lots of vessels.
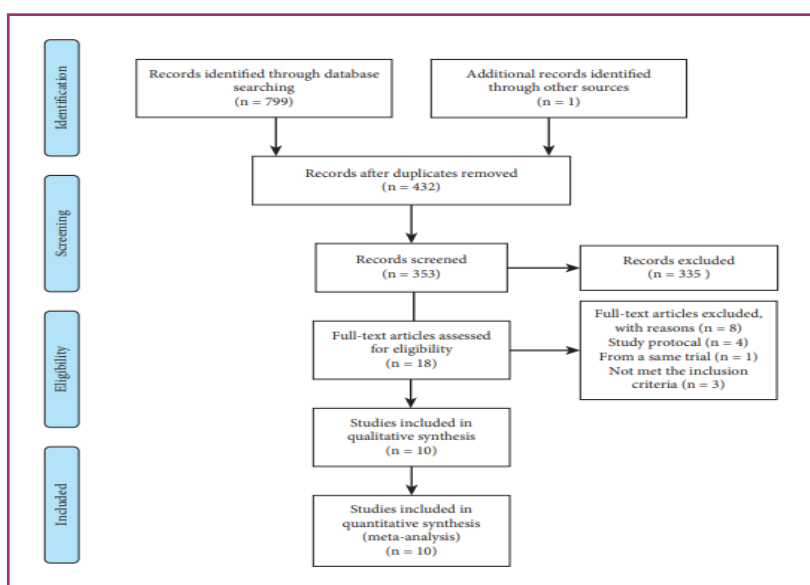

Figure 1: Flow Diagram of Literature Search

Table 1. Characteristics of the Rigors Included.

Study	No. of Patients	Patients	Randomization	Types of Stent	Time of Tirofiban	Follow-up Duration
. 27	400	With CS	Treatment with tirofiban (n = 200) against a placebo (n = 200)	BMS	Before PCI	30 days 6 months
22	483	No CS	(N = 241) Tirofiban and (N = 242) Placebo	BMS	Before angiography	A Time Period of Thirty Days, Plus Six Months
l. 4	300	With CS	Tirofiban (n = 149) vs. placebo (n = 151)	BMS	Before angiography	30 days Duration: 6 months

Study	No. of Patients	Patients	Randomization	Types of Stent	Time of Tirofiban	Follow-up Duration
23	119	No CS	Tirofiban (n = 30) vs. placebo (n = 89)	—	Before PCI	In-hospital 30 days
. 3	401	—	Tirofiban (n = 201) vs. placebo (n = 200)	BMS	—	30 days 1 year
. 25	200	—	Tirofiban (n = 102) vs. placebo (n = 98)	BMS	—	14 days 30 days
. 28	60	No CS	Tirofiban (n = 30) vs. placebo (n = 30)	BMS	Before PCI	30 days 6 months
26	2082	No CS	Tirofiban (n = 1052) vs. placebo (n = 1030)	BMS	—	30 days 1 year
. 24	800	No CS	Study of Tirofiban (n = 401) vs. Placebo (n = 399)	BMS DES	Before angiography	30 days
29	163	With CS	Tirofiban (n = 112) vs. placebo (n = 51)	BMS	Both	In-hospital 6 months

CS: cardiac shock; BMS: bare-steel stent; DES: drug-eluting stent; PCI, percutaneous coronary intervention.

Table 2. Outcomes of the Rigors Included.

Study	The Primary Outcomes	The Secondary Outcomes	The Safety Outcomes
Antoniucci et al. 27	A sum of all deaths, recurrent heart attacks, transient ischemic attacks, and strokes during a month	ST-segment improvement, cTFC after the procedure, infarct size at one month, mortality from any cause, death plus reinfarction, and TVR after six months	—
Brener et al. 22	At 6 months, death, reinfarction, or any TVR	A premature demise, recurrent infarction, or the need for emergency TVR	Bleeding
Ernst et al. 23	Recurrent MI	—	Bleeding
Mehilli et al. 24	SPECT-determined infarct size	Cause-specific mortality, myocardial infarction recurrence, cerebrovascular accident, need for emergent thoracic vascular surgery, and the frequency of bleeding problems	Bleeding
Montalescot et al. 4	A combination of fatalities, recurrent infarctions, and the need for immediate TVR	Death, recurrent infarction, or transient vascular occlusion at 30 and 6 months	Bleeding
Neumann et al. 25	When comparing baseline and 14-day follow-up, both papaverine-induced coronary flow velocity and wall motion index showed significant changes.	Thirty-day mortality, nonfatal reinfarction, and transient ventricular repolarization rates for unfavourable cardiac events	—

Study	The Primary Outcomes	The Secondary Outcomes	The Safety Outcomes
Neumann et al. 3	Late occurrence of loss; death, repeated MI, and TVR	TVR, repeated MI, and nonfatal deaths	—
Petronio et al. 28	Commonness of left ventricular remodelling at 6 months	The frequency of angiographic no-reflow after angioplasty, the final corrected time-to-flow curve, and the percentage change in LVEDV after six months	—
Tcheng et al. 26	The incidence of mortality, reinfarction, urgent repeat TVR, or disability at 30 days or 12 months	—	Bleeding
Zorman et al. 29	The combination of cardiac arrest, respiratory arrest, and the need for emergency TVR	—	—

Quality Assessment

Only randomised managed trials (RCTs) have been protected on this meta-analysis, and the hazard of bias in every studies changed into assessed the usage of a technique advanced via way of means of the Cochrane Collaboration. Results of an intensive exam of first-class are given (Supplementary Figure 1). Five out of 7 trials have been now no longer blindfolded, and have been most effective in part blinded, elevating the hazard of bias for performance. All trials had a low hazard of bias for selection, detection, and reporting. Lack of statistics on scientific consequences additionally expanded the chance of bias for attrition in five research.

A score of the reliability of the proof for every end result is shown. High-first-class proof changed into determined for 30- and 6-month all-reason mortality, recurrent MI, repeat revascularization, very last TIMI float three, and transfusion, even as moderate-first-class proof changed into determined for fundamental and minor bleeding and thrombocytopenia.

We do a TSA on each capacity outcome. The curves for each recurrent revascularization and thrombocytopenia have been steeper than predicted, while the curve for all-reason mortality at six months surpassed each the traditional and TSA cutoff. There changed into a discrepancy among the projected pattern length and the traditional boundary, the TSA border, and the curves for all-reason dying at 30 days, widespread bleeding, and transfusions. P values for Begg`s and Egger's assessments have been extra than 0.05, displaying that there has been no book bias, and the funnel plot indicated a ordinary distribution.

The Efficacy Outcomes

There is excessive heterogeneity among the 2 companies (2.4 percentage vs. 3.0 percentage, RR 0.81, 0.56-1.13, P=0.19, I3 = 0%, PHeterogeneity=0.75), no matter the truth that the 30-day all-reason dying fee is decrease withinside the tirofiban organization. Data in this degree are to be had from seven research. Deaths from any reason have been evaluated at 6 months in four of the ten research; withinside the tirofiban organization, it changed into appreciably decrease than withinside the placebo organization (four.1.2% vs. 7.1%, RR 0.58, 0.37-0.91, P=0.02, I2 = 0%, PHeterogeneity=0.50).

Eight research have suggested at the hazard of MI recurrence following revascularization. The chance of getting a 2nd MI or wanting revascularization changed into appreciably decreased withinside the tirofiban organization in comparison to the manipulate organization (four.6% vs 2.6%, RR 0.58, 0.43-0.78, P=0.0004,

I2 = 0%, PHeterogeneity=0.91). Furthermore, eight research determined a statistically widespread distinction among the 2 companies while analyzing the end result of very last TIMI float three (6.0% vs. eight%, RR 0.77, 0.62-0.96, P=0.02I2 = 18%, PHeterogeneity=0.29).

The Safety Outcomes and Sensitivity Analysis

There became proof of bleeding, each most important and moderate, in 5 investigations. Both businesses had nearly the identical wide variety of most important bleeding events (3.9% vs. 2.4%, RR 1.37, 0.93 to 2.03%, P=0.11, I2 = 15%, PHeterogeneity=0.32). Comparing the tirofiban and placebo businesses, the ones on tirofiban have been much more likely to have minor bleeding events (7.4% vs. five.4%; RR 1.29, 1.02-1.63; P=0.04; I2 = 67%; PHeterogeneity=0.02). The effects of youth bleeding various somewhat, however have been regularly constant. Excluding statistics from this take a look at decreased the discovered variety in results for mild bleeding (I2 = 42%, PHeterogeneity=0.16), as proven via way of means of the sensitivity evaluation. Difference among businesses is statistically good sized even at age 26 (13% vs. 7.9%, RR 1.60, 1.23-2.10, P=0.0006). There have been five research that checked out thrombocytopenia, and the effects confirmed that the ones the usage of tirofiban had a more threat of the aspect effect (4.9 percentage vs. 2.4 percentage, RR 2.05, 1.41-2.98, P=0.0003, I2 = 1%, PHeterogeneity=0.40). Overall, there has been no statistically good-sized distinction withinside the transfusion fees among the 2 businesses for the duration of all 6 trials (5.5 percentage vs. 4.5 percentage, relative threat 1.23, 0.90 four to 1.61, P=0.13, I2 = 0%, PHeterogeneity=0.42).

The Meta-Regression Analysis and Subgroup Analyses

Patients who skilled cardiac surprise have been labeled as excessive threat, even as folks that did now no longer have been labeled as low threat; a meta-regression evaluation became finished primarily based totally on book year, pattern length (trials with greater than 1,000 sufferers have been taken into consideration large, even as people with four hundred to 1,000 have been taken into consideration medium sized), affected person classification, and remedy duration (earlier than coronary angiography or earlier than PCI however after coronary angiography). The length of the samples utilised to examine the prevalence of youth bleeding may also account for discovered variations.

The antiplatelet approach lets in for subgroup research of each most important and minor bleeding. Clopidogrel use became now no longer related to an improved threat of most important bleeding (1.6% vs. three.9%, RR 0.58, 0.23-1.46, P=0.25, I2 = 57%, PHeterogeneity = 0.13). Dyspnea and a better threat of excessive haemorrhage have been visible with ticagrelor as compared to clopidogrel. However, there has been no statistically good-sized distinction withinside the prevalence of moderate bleeding among the clopidogrel and ticagrelor businesses.

Discussion

The relative chance of loss of life from any motive became decreased through 21% withinside the first 30 days and through 43% withinside the first 6 months, consistent with a meta-evaluation. The anti-aggregation impact of tirofiban on platelets might also additionally closing for some days after management 30; however, the healing advantage might also additionally bear for months, if now no longer years (Des Kölner Infarkt Modells, (n.d). Clinical research indicated that distal embolization improved the infarct size, left ventricular ejection fraction, and mortality chance in sufferers. Tirofiban gives long-time period blessings further to its short-time period blessings (improved coronary heart perfusion and much less distal embolization). However, handiest 20% of sufferers with this syndrome had distal embolization detected through angiography. Patients with anterior or multivessel sickness and beyond MI are much more likely to have distal embolization,

consequently tirofiban`s remedy on this institution can be beneficial. The aggregate of antiplatelet medicinal drugs is not unusual place practise, despite the fact that its results are unclear. Studying the effectiveness of tirofiban in aggregate with twin antiplatelet remedy for sufferers liable to distal embolization is consequently essential. The very last TIMI float became progressed through 23%, the chance ratio for a 2nd MI became decreased through 45%, and the want for revascularization became reduce in half. Since the curve of recurrent MI and very last TIMI float (3) did now no longer surpass the TSA boundary, extra randomised managed trials are had to acquire the essential pattern size.

The findings show that withinside the tirofiban institution, the chance ratio for predominant bleeding became 37% more than withinside the manipulate institution (Wang, C., Xia, Q., 2022).

Like the outcomes of any other meta-evaluation, tirofiban might also additionally boom the probability of significant bleeding. Possible reasons for the shortage of statistical importance consist of discrepancies withinside the definition of extreme bleeding throughout research. Subgroup evaluation showed the outcomes of earlier research displaying that ticagrelor became connected to a more chance of predominant bleeding as compared to clopidogrel. When examined with PHeterogeneity > 0.1, tirofiban became proven to boom the chance of sweet sixteen bleeding (P=0.0007). Mild bleeding became additionally seldom studied, with simply 5 research together with 3784 sufferers handiest 3 of which have been double-blind). Small pattern sizes in character research and inside sufferers may make a contribution to found variability. Transfusions appeared to be extra not unusual place withinside the tirofiban institution, however the records became ambiguous. Although Ernst et al determined that transfusions have been related to widespread bleeding, maximum research did now no longer consist of this information. This meta-evaluation determined that tirofiban's chance of inflicting thrombocytopenia doubled. Based on

those findings, it became decided that absolutely the chance of growing thrombocytopenia might boom through 2.5%, with a corresponding range required to damage of 40. One in 40 sufferers dealt with tirofiban will expand thrombocytopenia. Only while extreme thrombocytopenia develops, with a platelet rely of much less than 20,000/L 36, is discontinuation a possibility.

Because they're primarily based totally at the observations of many distinct varieties of people, the conclusions of this meta-evaluation have to be used with care. Because no people on this examine had risky angina or non-ST-phase elevation myocardial infarction, it`s feasible that the drug's efficacy can also additionally have modified relying at the sort of coronary heart assault the affected person had. Because tirofiban become advocated for early coronary intervention on this cohort we observed findings that had been distinct from the ones visible in preceding investigations of people with comparable problems (Perivoliotis, K., Sioka, et. al, 2018). Triosifiban differs from the opposite GPIs in its chemical shape at role 39, specifically abciximab and eptifibatide. Clinical research evaluating tirofiban to abciximab had conflicting effects. Because of this, we cannot actually enlarge those consequences to the formerly indicated populace or to different GPIs.

Limitations

The gift meta-evaluation of randomised scientific trials can also additionally have huge limitations. Firstly, there'll continually be discrepancies in examine to examine as regards to subjects like symptom duration, predominant endpoint design, and final results definition. The examine's credibility is in addition faded on account that most effective 3 of the pains utilised a double-blind design; the others had been both single-blind or open-label. Furthermore, facts on 1/2 of the occasions become lacking or partial, and now no longer all research had the essential scientific effects to be had for our evaluation. Lastly, facts from the TSA indicated that effects such as all-motive mortality at 30 days, very last TIMI glide 3, foremost bleeding, mild bleeding, and

transfusion did now no longer surpass the TSA boundary, suggesting that those measurements can be inaccurate. Finally, the papers hired on this meta-evaluation are of doubtful quality, and there's inadequate proof of the effect of tirofiban in a twin antiplatelet scenario. Therefore, in addition scientific research are had to verify the drug's usefulness withinside the gift day.

Conclusions

Tirofiban decreases the hazard of short-time period all-motive mortality, recurrent MI, repeat revascularization, and improves myocardial perfusion in sufferers with STEMI following PCI, in step with a latest systematic overview and meta-evaluation, however it additionally will increase the hazard of mild bleeding and thrombocytopenia.

References

Alkhatib, A., Sunoqrot, M., Hussien, A., Sayed, A., & Abdelhakim, A. (2022). Efficacy of Intracoronary versus Intravenous Abciximab in Cardiac Inflammatory Markers and Cardiac Function in Myocardial Infarctionn Patients. *Authorea Preprints*.

Allencherril, J., Alam, M., Levine, G., Jneid, H., Atar, D., Kloner, R. A., & Birnbaum, Y. (2018). Do We Need Potent Intravenous Antiplatelet Inhibition at the Time of Reperfusion During ST-Segment Elevation Myocardial Infarction? *Journal of Cardiovascular Pharmacology and Therapeutics*, *24*(3), 215–224. https://doi.org/10.1177/1074248418812167

Badescu, M. C., Ciocoiu, M., Rezus, E., Badulescu, O. V., Tanase, D. M., Ouatu, A., Dima, N., Ganceanu-Rusu, A. R., Popescu, D., Seritean Isac, P. N., Genes, T. M., & Rezus, C. (2021). Current Therapeutic Approach to Acute Myocardial Infarction in Patients with Congenital Hemophilia. *Life*, *11*(10), 1072. https://doi.org/10.3390/life11101072

Bai, N., Niu, Y., Ma, Y., Shang, Y. S., Zhong, P. Y., & Wang, Z. L. (2022). Evaluate Short-Term Outcomes of abciximab in ST-Segment Elevation Myocardial Infarction Patients Undergoing Percutaneous Coronary Intervention: A Meta-Analysis of Randomized Clinical Trials. *Journal of Interventional Cardiology*, *2022*.

Bentur, O. S., Li, J., Jiang, C. S., Martin, L. H., Kereiakes, D. J., & Coller, B. S. (2021). Application of Auxiliary VerifyNow Point-of-Care Assays to Assess the Pharmacodynamics of RUC-4, a Novel αIIbβ3 Receptor Antagonist. *TH Open*, *05*(03), e449–e460. https://doi.org/10.1055/s-0041-1732343

Des Kölner Infarkt Modells, K. I. M., & Streller, L. A. (n.d). *Aus dem Zentrum für Innere Medizin der Universität zu Köln Klinik und Poliklinik für Innere Medizin III Kardiologie Direktor: Universitätsprofessor Dr. med. St. Baldus.*

Fagel, N. D. (2022). *Invasive strategies in patients with acute coronary syndrome.*

Jakubiak, G. K., Pawlas, N., Cieślar, G., & Stanek, A. (2021b). Pathogenesis and Clinical Significance of In-Stent Restenosis in Patients with Diabetes. *International Journal of Environmental Research and Public Health*, *18*(22), 11970. https://doi.org/10.3390/ijerph182211970

James, S., Koul, S., Andersson, J., Angerås, O., Bhiladvala, P., Calais, F., Danielewicz, M., Fröbert, O., Grimfjärd, P., Götberg, M., Henareh, L., Ioanes, D., Jensen, J., Linder, R., Lindroos, P., Omerovic, E., Panayi, G., Råmunddal, T., Sarno, G., . . . Erlinge, D. (2021). Bivalirudin Versus Heparin Monotherapy in ST-Segment–Elevation Myocardial Infarction. *Circulation: Cardiovascular Interventions*, *14*(12). https://doi.org/10.1161/circinterventions.120.008969

Karathanos, A., Lin, Y., Dannenberg, L., Parco, C., Schulze, V., Brockmeyer, M., & Wolff, G. (2019). Routine glycoprotein IIb/IIIa inhibitor therapy in ST-segment elevation myocardial infarction: a meta-analysis. *Canadian Journal of Cardiology*, *35*(11), 1576-1588.

Kingma, J. G. (2018). Myocardial Infarction: An Overview of STEMI and NSTEMI Physiopathology and Treatment. *World Journal of Cardiovascular Diseases*, *08*(11), 498–517. https://doi.org/10.4236/wjcd.2018.811049

Onishi, A., Omae, K., Luo, Y., Imai, H., Takahashi, S., Itaya, T., Pinson, C., Nevitt, S. J., & Furukawa, T. A. (2020). No consistent evidence of data availability bias existed in recent individual participant data meta-analyses: a meta-epidemiological study. *Journal of Clinical Epidemiology*, *118*, 107-114.e5. https://doi.org/10.1016/j.jclinepi.2019.10.004

Perivoliotis, K., Sioka, E., Katsogridaki, G., & Zacharoulis, D. (2018a). Laparoscopic Gastric Plication versus Laparoscopic Sleeve Gastrectomy: An Up-to-Date Systematic Review and Meta-Analysis. *Journal of Obesity*, *2018*, 1–14. https://doi.org/10.1155/2018/3617458

Somaschini, A., Cornara, S., Ferlini, M., Crimi, G., Camporotondo, R., Gnecchi, M., Ferrario Ormezzano, M., Oltrona Visconti, L., De Ferrari, G. M., & De Servi, S. (2019). Favorable effect of glycoprotein IIbIIIa inhibitors among STEMI patients treated with primary PCI and incomplete ST resolution. *Platelets*, *31*(1), 48–54. https://doi.org/10.1080/09537104.2018.1562171

Tavenier, A. H., Hermanides, R. S., Fabris, E., Lapostolle, F., Silvain, J., ten Berg, J. M., Lassen, J. F., Bolognese, L., Cantor, W. J., Cequier, N., Chettibi, M., Goodman, S. G., Hammett, C. J., Huber, K., Janzon, M., Merkely, B., Storey, R. F., Zeymer, U., Ecollan, P., . . . van t Hof, A. W. J. (2019). Efficacy and Safety of Glycoprotein IIb/IIIa Inhibitors on Top of Ticagrelor in STEMI: A Subanalysis of the ATLANTIC Trial. *Thrombosis and Haemostasis*, *120*(01), 065–074. https://doi.org/10.1055/s-0039-1700546

Verdoia, M., Kedhi, E., Suryapranata, H., & De Luca, G. (2019). Ticagrelor in the prevention of coronary and non-coronary atherothrombotic events: A comprehensive meta-analysis of 10 randomized trials. *Atherosclerosis*, *284*, 136–147. https://doi.org/10.1016/j.atherosclerosis.2019.02.011

Vlachojannis, G. J., Vogel, R. F., Wilschut, J. M., Lemmert, M. E., Delewi, R., Diletti, R., van Vliet, R., van der Waarden, N., Nuis, R. J., Paradies, V., Alexopoulos, D., Zijlstra, F., Montalescot, G., Angiolillo, D. J., Krucoff, M. W., Van Mieghem, N. M., & Smits, P. C. (2020). COMPARison of pre-hospital CRUSHed vs. uncrushed Prasugrel tablets in patients with STEMI undergoing primary percutaneous coronary interventions: Rationale and design of the COMPARE CRUSH trial. *American Heart Journal*, *224*, 10–16. https://doi.org/10.1016/j.ahj.2020.03.005

Wang, C., Xia, Q., Hu, B., Jiang, W., & Zhang, H. (2022). The Effectiveness and Safety of Huangqi Xixin Decoction for Cough Variant Asthma: A Systematic Review and Meta-Analysis. *Evidence-Based Complementary and Alternative Medicine*, *2022*, 1–12. https://doi.org/10.1155/2022/9492100

Wang, J. (n.d). *From the Clinic for Cardiology of University of Lübeck Director: Prof. Dr. med. Ingo Eitel.*