Sympathectomy Peripheral Artery Disease: Systematic Review with ☸SAIMSARA.

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Abstract: This paper aims to systematically review the available evidence on sympathectomy in peripheral artery disease, synthesizing findings on its efficacy, clinical applications, and associated factors to identify current knowledge gaps and future research directions. The review utilises 36 studies with 170679 total participants (naïve ΣN). Lumbar sympathectomy surgery resulted in a 59% increase in arterial diameter and a 201% increase in perfusion compared with sham surgery in Sprague-Dawley rats. While this animal data suggests significant physiological benefits, the generalizability to human peripheral artery disease is limited by the scarcity of comparable quantitative efficacy data in human studies. The most significant limitation affecting certainty is the limited human efficacy data, which largely consists of qualitative observations or small, uncontrolled studies. Therefore, a concrete next step involves conducting large-scale, randomized controlled trials to definitively establish the efficacy and safety of sympathectomy in specific human PAD populations, such as those with chronic limb-threatening ischemia or Buerger's disease.

Keywords: Sympathectomy; Peripheral Artery Disease; Lumbar Sympathectomy; Chronic Limb Ischemia; Is

Review Stats

- Generated: 2026-02-02 23:21:15 CET
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- Source: Semantic Scholar
- Scope: All fields
- Keyword Gate: Fuzzy (≥60% of required terms, minimum 2 terms matched in title/abstract)
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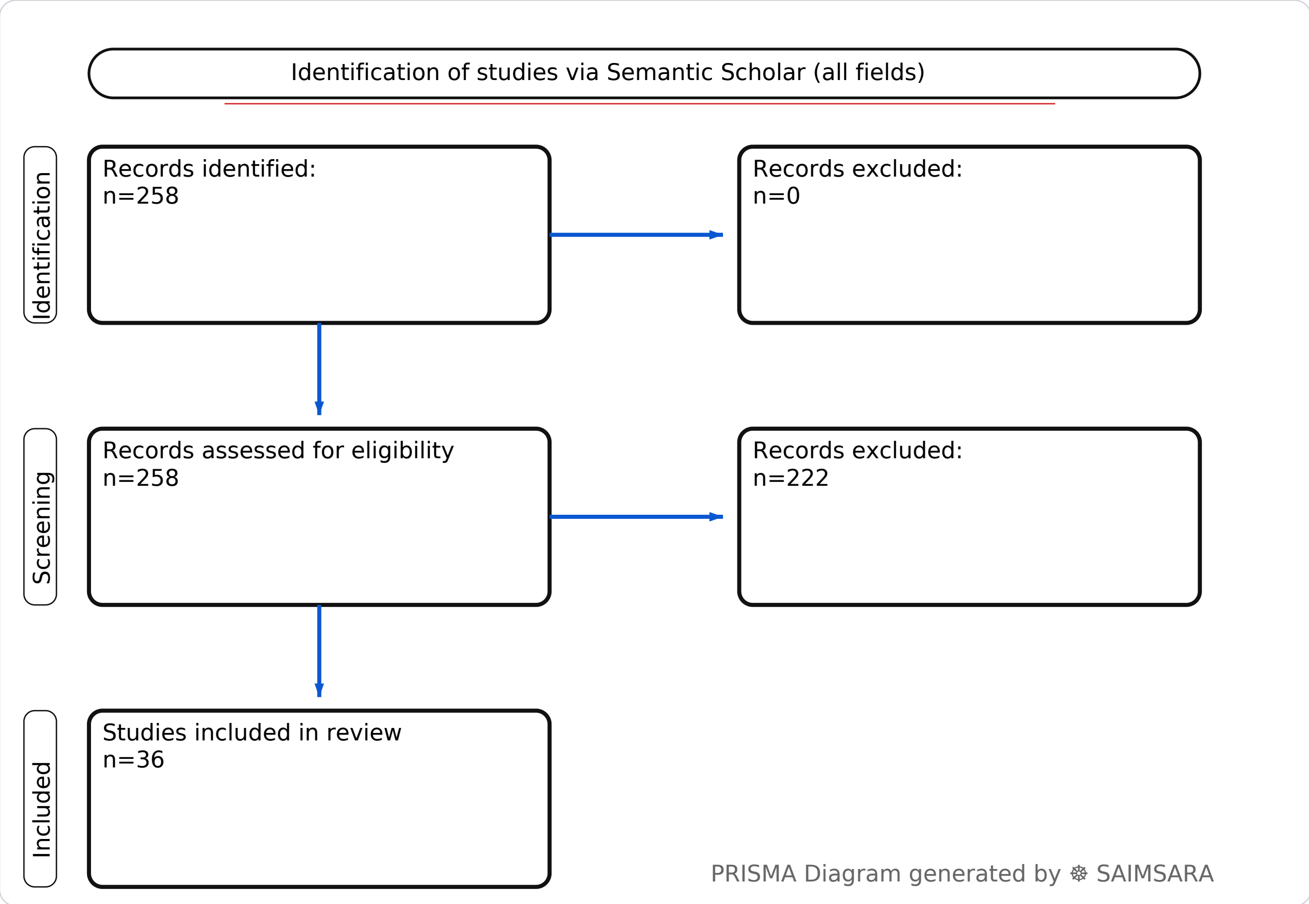
- Included original Abstracts/Papers: 36
- Total study participants (naïve ΣN): 170679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Records excluded:
n=0
Screening
Records assessed for eligibility
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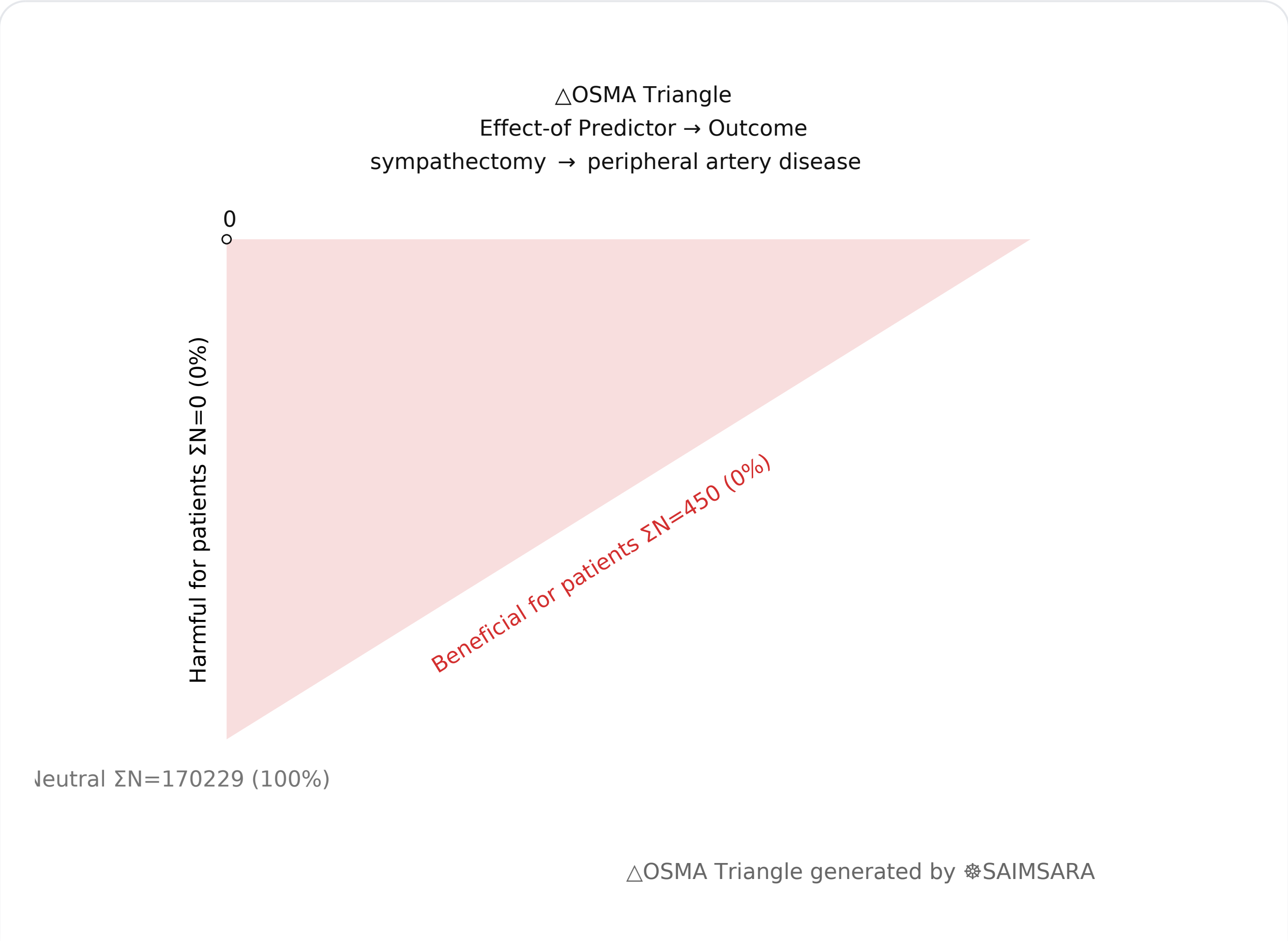
Records excluded:
n=222
Included
Studies included in review
n=36
PRISMA Diagram generated by ☸ SAIMSARA


△OSMA Triangle
Effect-of Predictor → Outcome
sympathectomy → peripheral artery disease
0
Harmful for patients ΣN=0 (0%)
Beneficial for patients ΣN=450 (0%)
Neutral ΣN=170229 (100%)
△OSMA Triangle generated by ☸SAIMSARA

Outcome-Sentiment Meta-Analysis (OSMA): *(LLM-only)*

Frame: Effect-of Predictor → Outcome • *Source*: Semantic Scholar

Outcome: peripheral artery disease Typical timepoints: peri/post-op, 1-y. Reported metrics: %, CI, p.

Common endpoints: Common endpoints: mortality, complications, admission.

Predictor: sympathectomy — exposure/predictor. Typical comparator: sham surgery, sham, control, heart failure patients with no....

- **1) Beneficial for patients** — peripheral artery disease with sympathectomy — [17] — ΣN=450
- **2) Harmful for patients** — peripheral artery disease with sympathectomy — — — ΣN=0
- **3) No clear effect** — peripheral artery disease with sympathectomy — [1], [2], [3], [4], [5], [6], [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [18], [19], [20], [21], [22], [23], [24], [25], [26], [27], [28], [29], [30], [31], [32], [33], [34], [35], [36] — ΣN=170229

1) Introduction

Peripheral artery disease (PAD) represents a significant global health burden, characterized by stenoses or occlusions in arteries supplying the limbs, often leading to chronic limb-threatening ischemia (CLTI) and a high risk of amputation [3, 22, 23]. PAD is frequently associated with other cardiovascular diseases, increasing the risk of adverse events such as stroke and mortality [7, 18, 22]. While conventional treatments include lifestyle modifications, medical management, and revascularization, a substantial proportion of patients still face severe outcomes, including amputation [3]. Sympathectomy, a procedure aimed at disrupting sympathetic nerve pathways, has historically been considered for improving limb perfusion in various peripheral vascular conditions, including thromboangiitis obliterans (Buerger's disease) and occlusive PAD [10, 21, 23, 29, 31, 35]. This paper synthesizes the current understanding of sympathectomy in the context of PAD, drawing from recent findings on its mechanisms, efficacy, and associated clinical considerations.

2) Aim

This paper aims to systematically review the available evidence on sympathectomy in peripheral artery disease, synthesizing findings on its efficacy, clinical applications, and associated factors to identify current knowledge gaps and future research directions.

3) Methods

Systematic review with multilayer AI research agent: keyword normalization, retrieval & structuring, and paper synthesis (see SAIMSARA About section for details).

- **Bias:** The qualitative assessment of study designs indicates a notable prevalence of cohort, cross-sectional, and mixed-design studies, with several lacking specified study designs or directionality [1, 3, 4, 5, 6, 7, 8, 9, 12, 13, 14, 15, 16, 17, 18, 19, 22, 24, 25, 26, 27, 32, 33, 34, 36]. Experimental studies are rare and primarily animal-based [2]. The frequent absence of control groups, small sample sizes in sympathectomy-focused studies, and reliance on retrospective or observational data introduce potential for selection bias and limit the generalizability and causal inference of findings related to sympathectomy's direct efficacy in humans.

4) Results

4.1 Study characteristics: The included studies comprise a diverse range of designs, including cohort, experimental, cross-sectional, and mixed studies, with several not specifying their design. Populations varied from chronic limb-threatening ischemia (CLTI) patients to Sprague-Dawley rats, lower extremity peripheral artery disease (LE-PAD) patients, and large general population cohorts. Follow-up periods ranged from 1 week to 18 years, with many studies not reporting follow-up duration.

4.2 Main numerical result aligned to the query:

Lumbar sympathectomy surgery resulted in a 59% increase in arterial diameter and a 201% increase in perfusion compared with sham surgery in Sprague-Dawley rats [2]. While direct comparable numerical efficacy metrics for sympathectomy in human peripheral artery disease are not consistently reported across studies, qualitative findings suggest that sympathectomies yield good results in early stages of thromboangiitis obliterans and vasospastic disease [10] and are a method for improvement of lower limb perfusion in occlusive peripheral artery disease [23]. However, one study noted that sympathectomy may not be more effective in treating Buerger's disease than cigarette smoking cessation or pharmaceutical therapy [16].

4.3 Topic synthesis:

- **Sympathectomy Efficacy and Mechanisms**: Lumbar sympathectomy increased arterial diameter by 59% and perfusion by 201% in rats [2]. Clinically relevant temperature increases were observed via infrared thermography in dermatomes corresponding to occluded angiosomes post-interventional lumbar sympathectomy in CLTI patients [1]. Sympathectomy is described as a method for improving lower limb perfusion in occlusive

PAD [23] and a surgical intervention for limb salvage in Buerger's disease [30, 35].

- **Sympathectomy Modalities and Application**: Lumbar sympathectomy is a traditional surgical approach for limb ischemia and peripheral vascular disease [31], performed in 8.6% of LE-PAD patients in one study [3]. Minimally invasive chemical destruction of lumbar sympathetic ganglia under CT control offers comparable effectiveness to surgical lumbar sympathectomy for obliterating diseases of the extremities [11]. Endoscopic thoracal ganglion sympathectomy has also been performed for Buerger's disease [20].
- **Peripheral Artery Disease Prevalence and Risk Factors**: Elevated remnant cholesterol was associated with an increased risk of PAD in individuals with diabetes (HR 1.6, 95% CI 1.1–2.3) [9]. Higher serum MFAP4 levels were associated with increased odds of critical lower-extremity ischemia (OR 2.65, $p < 0.001$) [5]. Several plasma biomarkers, including Lp-PLA2, CRP, copeptin, N-BNP, and cystatin C, were associated with incident symptomatic lower extremity arterial disease (HRs ranging from 1.19 to 1.59) [6]. Increased carbamylated albumin levels were associated with increased incidence of PAD [19], and an LDLR missense variant was linked to increased PAD risk (HR 1.69, 95% CI 1.01-2.82) [27].
- **PAD Comorbidities and Mortality**: PAD was associated with a higher 1-year rate of ischemic stroke (HR 1.34, 95% CI 1.08–1.65) and all-cause death (HR 1.47, 95% CI 1.35–1.59) in heart failure patients [22]. In patients with coronary artery disease and PAD, there was significantly higher five-year all-cause mortality after TAVI [7]. Preoperative peripheral vascular disease was independently associated with perioperative stroke after coronary artery bypass grafting (CABG) [18]. PAD was also associated with an increased hazard ratio for cardiovascular-related readmission in heart failure patients [36].
- **PAD Management and Outcomes**: Despite lifestyle modification and medical management, amputation was required in 39.10% of PAD patients [3]. The incidence rate of lower extremity artery disease (LEAD) repair decreased in Denmark from 1996 to 2018 (IRR 0.70, 95% CI 0.66–0.75) [4]. Combined inhibition of Lp(a) and PCSK9 was associated with a pronounced reduction in atherosclerotic cardiovascular disease (ASCVD) and mortality risk, including PAD (OR 0.74, $p=0.0034$; OR 0.82, $p=5.9 \times 10^{-34}$) [17]. Sympathectomy may not be more effective than smoking cessation or pharmaceutical therapy in Buerger's disease [16].
- **Diagnostic and Prognostic Markers**: Infrared thermography is a new approach for evaluating interventional lumbar sympathectomy efficacy in CLTI patients [1]. Systemic MFAP4 was associated with primary patency after vascular reconstruction and the need for vascular reconstruction and mortality in PAD patients [34]. Plasma biomarkers (Lp-PLA2, CRP, copeptin, N-BNP, cystatin C) are associated with incident symptomatic LEAD [6].
- **Historical Context of Sympathectomy**: Lumbar sympathectomy has been a routine treatment for limb ischemia and peripheral vascular disease since at least 1999 [31], and was recommended for thrombo-angiitis in suitable cases as early as 1936 [35].

5) Discussion

5.1 Principal finding: The most direct numerical evidence for sympathectomy's efficacy comes from an animal model, where lumbar sympathectomy increased arterial diameter by 59% and perfusion by 201% compared to sham surgery [2]. While human data on quantitative efficacy is limited, qualitative reports support its role in improving lower limb perfusion and limb salvage in occlusive peripheral artery disease and Buerger's disease [10, 23, 30, 35].

5.2 Clinical implications:

- Sympathectomy should be considered as a therapeutic option for limb salvage in specific conditions such as Buerger's disease and occlusive peripheral artery disease, particularly when other revascularization strategies are not feasible or have failed [23, 30, 35].
- The use of infrared thermography can provide a non-invasive, objective method to evaluate the immediate efficacy of interventional lumbar sympathectomy, helping to guide treatment and identify areas of improved perfusion in CLTI patients [1].
- Minimally invasive chemical destruction of lumbar sympathetic ganglia presents a viable alternative to traditional surgical sympathectomy, potentially offering comparable effectiveness with reduced invasiveness for patients with obliterating diseases of the extremities [11].
- Given the high amputation rates (39.10%) observed in PAD patients despite conventional management [3], sympathectomy may play a crucial role in preventing limb loss in carefully selected individuals.
- The strong association of PAD with increased risks of ischemic stroke and all-cause mortality [7, 22] underscores the importance of comprehensive cardiovascular risk assessment and management, where sympathectomy could be part of a multimodal approach.

5.3 Research implications / key gaps:

- **Comparative Efficacy Trials** — Conduct randomized controlled trials comparing surgical and chemical sympathectomy against each other and against best medical therapy or revascularization in human PAD, using standardized limb salvage and perfusion endpoints. [11, 16]
- **Long-term Outcome Assessment** — Initiate prospective cohort studies with extended follow-up (e.g., >5 years) to evaluate the long-term impact of sympathectomy on limb function, re-amputation rates, and quality of life in CLTI patients. [3, 22]
- **Patient Selection Biomarkers** — Investigate the utility of novel biomarkers (e.g., MFAP4, C-Alb, Lp-PLA2) and advanced imaging (e.g., infrared thermography) to identify optimal candidates for sympathectomy and predict treatment response. [1, 5, 6, 19, 34]

- **Mechanistic Studies in Humans** — Perform studies to elucidate the precise neurovascular and cellular mechanisms by which sympathectomy improves perfusion and arterial diameter in human PAD, building upon animal model findings. [2]
- **Combination Therapy Strategies** — Explore the potential synergistic benefits of combining sympathectomy with emerging pharmacological therapies (e.g., Lp(a) and PCSK9 inhibitors) or advanced revascularization techniques in severe PAD. [17]

5.4 Limitations:

- **Limited Human Efficacy Data** — Direct numerical efficacy data for sympathectomy in human PAD is scarce, relying heavily on qualitative statements or animal models, limiting the certainty of its quantitative benefits.
- **Heterogeneous Study Designs** — The included studies vary widely in design, population, and endpoints, making direct comparisons and synthesis challenging.
- **Small Sample Sizes** — Several studies on sympathectomy involve very small sample sizes (e.g., N=2, N=4, N=25), which limits the generalizability and statistical power of their findings.
- **Lack of Control Groups** — Many studies describing sympathectomy's use lack robust control groups or direct comparisons against alternative treatments, hindering definitive conclusions about its comparative effectiveness.
- **Focus on Comorbidities** — A significant portion of the literature focuses on PAD as a comorbidity or risk factor for other cardiovascular events, rather than directly evaluating sympathectomy for PAD.

5.5 Future directions:

- **Randomized Controlled Trials** — Conduct large-scale RCTs to evaluate sympathectomy's efficacy against standard care for CLTI and Buerger's disease.
- **Standardized Outcome Measures** — Establish and utilize standardized outcome measures for limb salvage, perfusion, and pain relief in sympathectomy studies.
- **Biomarker-Guided Selection** — Develop and test algorithms for patient selection for sympathectomy based on novel biomarkers and imaging.
- **Longitudinal Cohort Studies** — Initiate prospective longitudinal cohort studies to track long-term functional and survival outcomes post-sympathectomy.
- **Cost-Effectiveness Analyses** — Perform economic evaluations to determine the cost-effectiveness of sympathectomy in the management of severe PAD.

6) Conclusion

Lumbar sympathectomy surgery resulted in a 59% increase in arterial diameter and a 201% increase in perfusion compared with sham surgery in Sprague-Dawley rats [2]. While this animal data suggests significant physiological benefits, the generalizability to human peripheral artery disease is limited by the scarcity of comparable quantitative efficacy data in human studies. The most significant limitation affecting certainty is the limited human efficacy data, which largely consists of qualitative observations or small, uncontrolled studies. Therefore, a concrete next step involves conducting large-scale, randomized controlled trials to definitively establish the efficacy and safety of sympathectomy in specific human PAD populations, such as those with chronic limb-threatening ischemia or Buerger's disease.

References

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Figure 1. Publication-year distribution of included originals

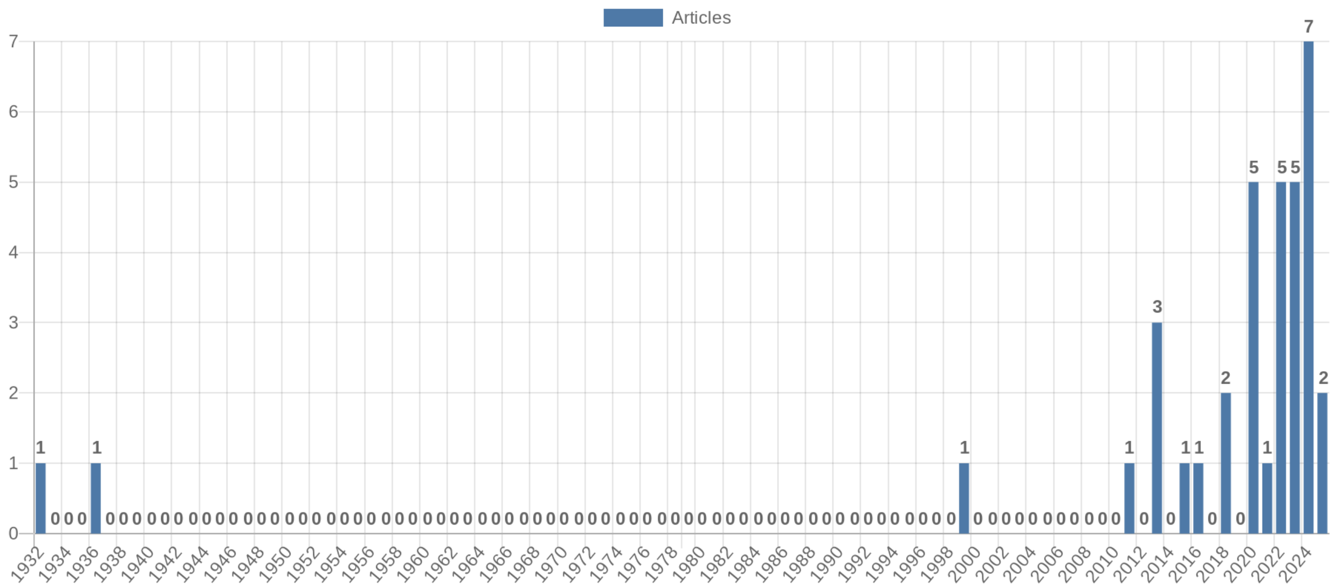

Figure 2. Study-design distribution of included originals

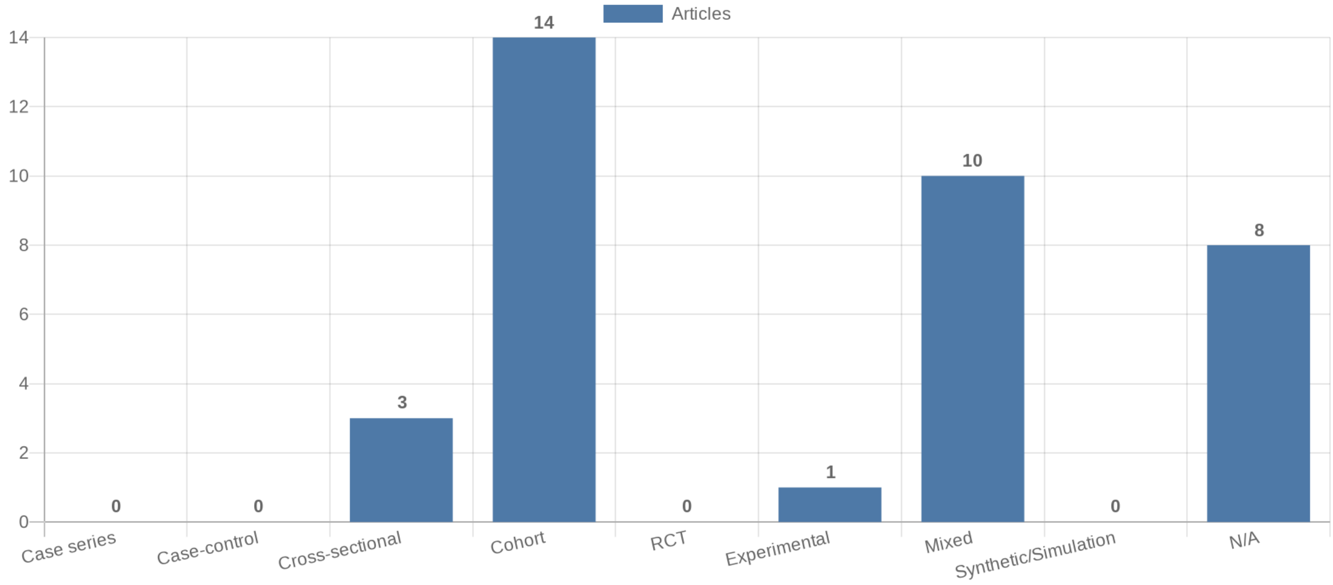

Figure 3. Study-type (directionality) distribution of included originals

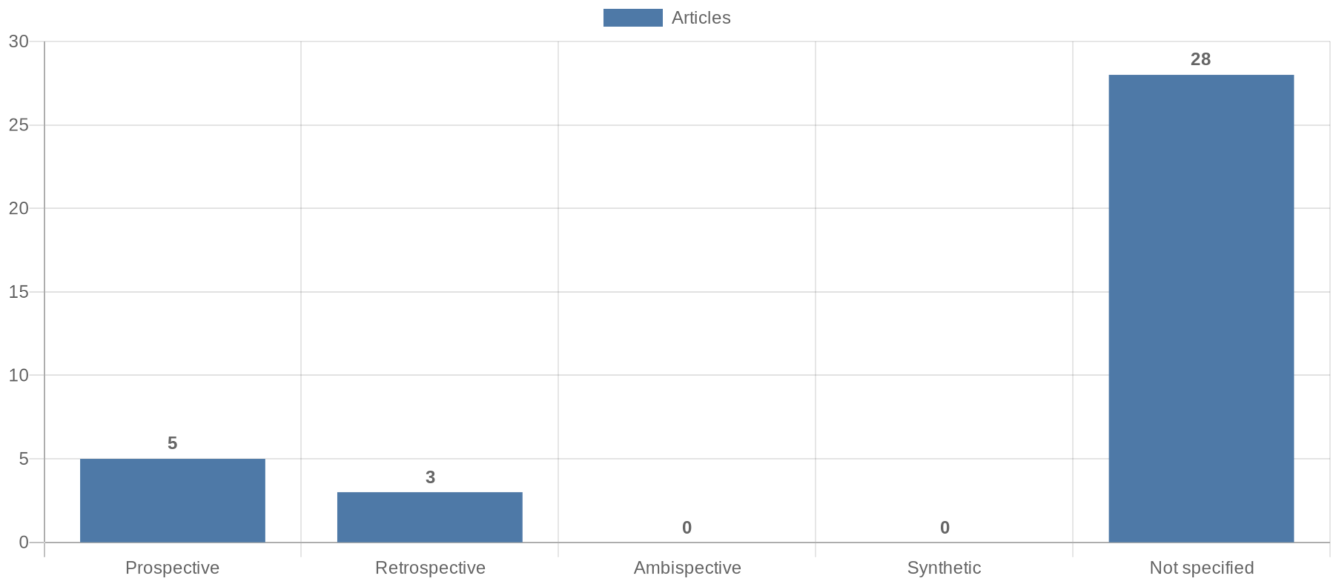

Figure 4. Main extracted research topics

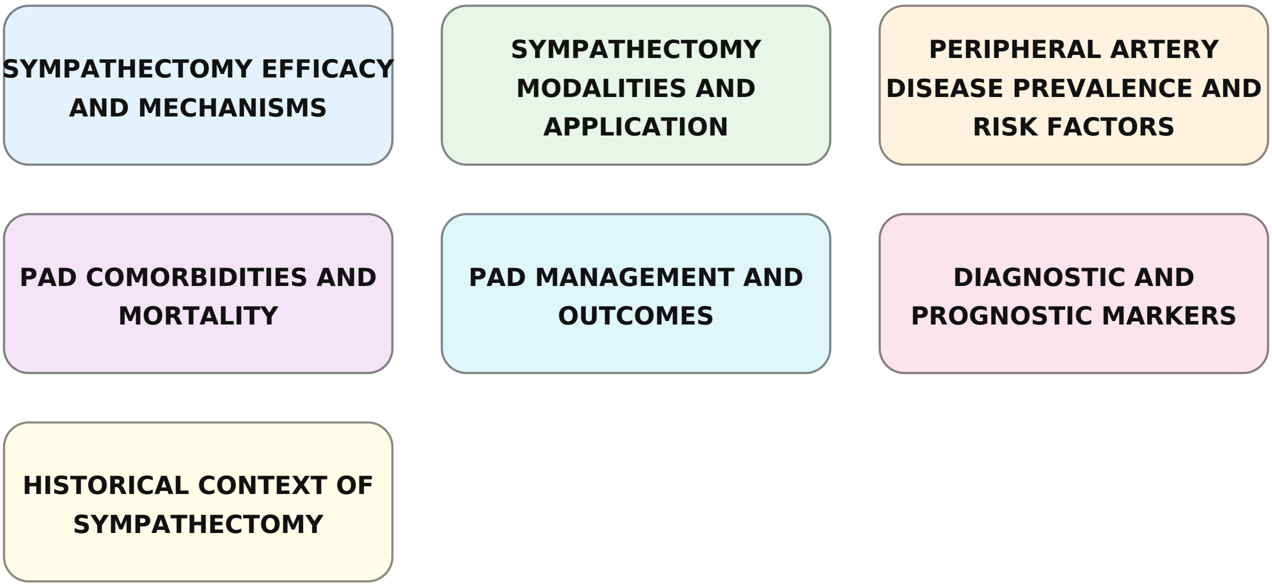

Figure 5. Limitations of current studies (topics)

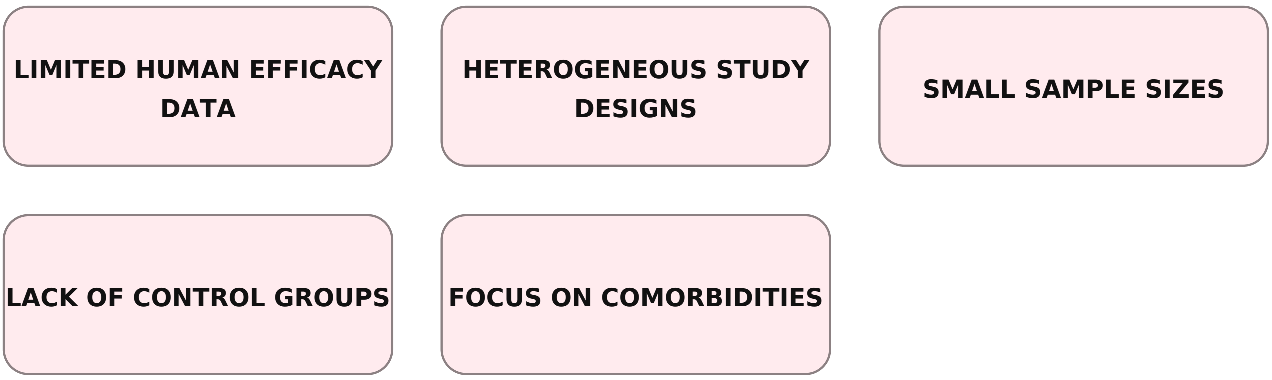

Figure 6. Future research directions (topics)