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INTEGRATED MASTER'S THESIS

Waiting Time and Predictors of Waiting Time for Transcatheter Aortic Valve Implantation in Patients With Severe Aortic Valve Stenosis

Perkateterinio aortos vožtuvo implantavimo pacientams su didelio laipsnio aortos vožtuvo stenoze laukimo laikas ir jį lemiantys veiksniai

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1. LIST OF ABBREVIATIONS

AoV – aortic valve.

AS – aortic valve stenosis.

AVR – aortic valve replacement.

BMI – body mass index.

COPD – chronic obstructive pulmonary disease.

CTA – computed tomography angiography.

ESC – European Society of Cardiology.

EuroSCORE II – European System for Cardiac Operative Risk Evaluation II.

EWT – evaluation waiting time.

HF – heart failure.

LVEF – left ventricular ejection fraction.

MDT – multidisciplinary team or heart team.

NYHA Classification – New York Heart Association Functional Classification of Heart Failure.

PAPS – systolic pulmonary artery pressure.

PWT – procedural waiting time.

SAVR – surgical aortic valve replacement.

TAVI – transcatheter aortic valve implantation.

TPVI – transcatheter pulmonary valve implantation.

TTE – transthoracic echocardiography.

TWT – total waiting time.

VUH SK – Vilnius University Hospital Santaros Klinikos.

Mdn – median.

M – mean.

Q1 – first quartile, corresponding to 25^{th} percentile.

Q3 – third quartile, corresponding to 75^{th} percentile.

IQR – interquartile range between first and third quartiles.

SD – standard deviation.

CI – confidence interval.

LR – logistic regression model.

OR – odds ratio.

HR – hazard ratio.

2. ABSTRACT

Introduction. Even though the global numbers of transcatheter aortic valve implantation (TAVI) increase yearly, the ageing population and expanding indications create the demand for TAVI, which is still unmet. Patients with diagnosed symptomatic severe aortic valve stenosis have a poor prognosis and increased mortality while being on the waiting list for aortic valve replacement therapy. This study aimed to evaluate the changes in TAVI waiting times from 2009 to 2024 in a tertiary centre and possible sociodemographic and health condition predictors of waiting times.

Methods. Retrospective single-centre analysis included TAVI cases (n=806) between 2009 and 2024. The primary outcome was total waiting time from the ultrasound diagnosis of severe aortic stenosis and documented indication for valve replacement. Secondary outcomes were evaluation waiting time (from diagnosis to the last pre-TAVI evaluation test) and procedural waiting time (from the last test to TAVI). For inferential analyses, Kruskal-Wallis and Mann-Whitney U tests were used for quantitative variables, and Chi-square and Fisher-Freeman-Halton Exact tests were used for categorical data. Predictors were modelled with logistic regression.

Results. 806 cases were analysed, of which 64.89 % were female and 85.36 % were 75 years or older. The total waiting time was a median of 189.5 days in 2009 – 2024 and a median of 173 days in 2021 – 2024. The evaluation waiting time was 62.5 days in 2009-2024 and 49 days in 2021-2024. The procedural waiting time was 78.5 days in 2009-2024 and 89.5 days in 2021-2024. In 2021, procedural waiting time surpassed evaluation waiting time, 70 and 66 days, respectively. In 2021-2024, total waiting time was shorter in patients with left ventricular ejection fraction below 30 % (58 days, $p < 0.001$), previous history of aortic valve surgery ($p = 0.028$), non-elective group (36 days, $p < 0.001$), previous myocardial infarction (145 days, $p = 0,005$), male patients (153 days, $p = 0.015$). Logistic regression showed age (OR 0.96; CI [0.929; 0.997]), year (OR 0.31; CI [0.176; 0.550] for 2022; OR 0.35; [0.2; 0.621] for 2023), non-elective TAVI (OR 0.09; CI [0.046; 0.189]), reason groups (OR 3.6; CI [1.972; 6.555] for health-related; OR 28.94; CI [10.815; 77.451] for personal reasons) to be significant predictors of waiting.

Conclusion. From 2021 to 2024, there was a trend of increasing total waiting time, driven by a growth in procedural waiting time, with total waiting time exceeding those described in the literature. Age, year, urgency, reasons for delay, and multiple other clinical factors appear to be important predictors of waiting times.

Key words. TAVI, Waiting Time, Severe Aortic Valve Stenosis.

SANTRAUKA

Įvadas. Nors pasaulyje kasmet atliekama vis daugiau perkateterinio aortos vožtuvo implantavimo (TAVI) intervencijų, senėjant visuomenei ir plečiantis indikacijoms, TAVI poreikis nuolat auga, tačiau vis dar nėra pakankamai patenkinamas. Pacientų, kuriems diagnozuota simptominė sunki aortos vožtuvo stenozė, prognozė yra prasta, o aortos vožtuvo keitimo laukimas yra susijęs su padidėjusiu mirtingumu. Šio tyrimo tikslas – įvertinti TAVI laukimo laiko dinamiką 2009 – 2024 m. tretinio lygio ligoninėje bei galimus sociodemografinius ir sveikatos būklės veiksnius, lemiančius trumpesnį ar ilgesnį laukimą.

Metodai. Retrospektyvinė vieno centro analizė apėmė 2009 – 2024 m. TAVI atvejus (n = 806). Pirminė baigtis buvo bendras laukimo laikas nuo didelio laipsnio aortos stenozės patvirtinimo ultragarsu ir dokumentuotos indikacijos vožtuvo keitimui. Antrinės baigtys buvo ištyrimo laukimo trukmė (nuo diagnozės nustatymo iki paskutinio TAVI reikalingo tyrimo) ir procedūros laukimo trukmė (nuo paskutinio tyrimo iki TAVI). Inferencinei analizei naudoti Kruskalo-Voliso ir Mano-Vitnio U testai kiekybiniams kintamiesiems, Chi kvadrato ir *Fisher-Freeman-Halton* tikslusis testai – kategoriniams duomenims. Predikciniai ryšiai buvo modeliuojami taikant logistinę regresiją.

Rezultatai. Į tyrimą įtraukti 806 atvejai, kurių 64,89 proc. sudarė moterys ir 85,36 proc. buvo 75 metų ir vyresni. Bendros laukimo trukmės mediana siekė 189,5 dienos 2009 – 2024 m. ir 173 dienas 2021 – 2024 m. Ištyrimo laukimo laiko mediana buvo 62,5 dienos 2009 – 2024 m. ir 49 dienos 2021 – 2024 m. Procedūros laukimo laiko mediana buvo 78,5 dienos 2009 – 2024 m. ir 89,5 dienos 2021 – 2024 m. 2021 m. procedūros laukimo trukmė viršijo ištyrimo laukimo trukmę ir atitinkamai siekė 70 ir 66 dienas. Bendras laukimo laikas 2021 – 2024 metais buvo trumpesnis pacientams, kurių kairiojo skilvelio išstūmio frakcija mažesnė nei 30 % (58 dienos, $p < 0,001$), buvo atlikta aortos vožtuvo operacija ($p = 0,028$), TAVI atlikta neplanine tvarka (36 dienos, $p < 0,001$), buvo persirgę miokardo infarktu (145 dienos, $p = 0,005$), vyrams (153 dienos, $p = 0,015$). Logistinė regresija parodė, kad amžius (OR 0,96; PI [0,929; 0,997]), metai (OR 0,31; PI [0,176; 0,550] 2022 m.; OR 0,35; [0,2; 0,621] 2023 m.), neplaninis TAVI (OR 0,09; PI [0. 046; 0,189]), priežasčių grupės (OR 3,6; CI [1,972; 6,555] susijusios su sveikata; OR 28,94; CI [10,815; 77,451] asmeninės) yra reikšmingi laukimo prognostiniai veiksniai.

Išvados. 2021 – 2024 metais stebėta bendro laukimo laiko didėjimo tendencija, lemta procedūros laukimo trukmės, o bendras laukimo laikas viršijo literatūroje aprašytas trukmes. Amžius, TAVI atlikimo metai, skubumas, atidėjimo priežastys bei kiti klinikiniai faktoriai yra svarbūs laukimo laiko veiksniai.

Raktažodžiai. TAVI, Laukimo laikas, Didelio laipsnio aortos vožtuvo stenozė.

3. INTRODUCTION

Aortic valve stenosis (AS) is already recognised as the leading heart valve disease in high-income settings (1), but its clinical burden and relevance continue to increase. Prevalence estimations highly depend on age group: AS was observed in 0.2 % of the research participants between 50 – 59 years old, and among the 80 – 89 year group, it reached 9.8 % (2). Severe AS is less frequent, ranging between 3.4 % and 4.3 % (3,4) in different studies.

Today, the main modes of intervention are surgical aortic valve replacement (SAVR), transcatheter aortic valve implantation (TAVI), and balloon aortic valvuloplasty as a bridging procedure (5). However, this has not always been the case. Over the past two decades, both the evidence and clinical applications of TAVI have evolved significantly: from the first implantation in human in 2002 (6) and absence from the 2007 ESC Guidelines for valvular heart disease (7) to being recognized as a tailored, equal alternative to SAVR for high-risk severe AS patient group in the 2021 guideline edition (5). The yearly cases of TAVI have steadily risen since 2011, and from 2013, TAVI volume exceeded SAVR in one of the most active adopters – Germany (8), from 2019 in the United States (USA) (9) and from 2020 in the UK (10). The composition of patients also shifted from prohibitive-risk and high-risk profiles until 2018 to intermediate-risk patients, who became the largest cohort later (11). Further development of indications might shift to asymptomatic severe AS or even moderate AS, as there is increasing evidence of the significance of these AS forms and the potential benefits of a timely intervention (12,13). The ageing population fosters the growth of TAVI demand as well. In 2007, when the first TAVI device was approved in the European Union (EU) (14), 17.1 % of the European population (16.6 % of Lithuanian) consisted of citizens 65 years and over; in 2023, it reached 21.3 % (20 % of Lithuanian), and it is estimated that this population will expand to 29.5 % in 2050 (31.5 % in Lithuania) (15). Naturally, AS prevalence is also expanding – in 1990, there were 1,732,988 calcific aortic valve disease cases, and by 2019, the number had increased by 443 %, whereas the incidence increased by 351 % (16).

TAVI disrupted the traditional workflow of AS management, requiring healthcare systems to adjust. Multiple quality indicators can be set to evaluate the adoption of TAVI (17), and considering the poor prognosis of untreated symptomatic severe AS (18), waiting times become of particular significance. There is growing evidence that implies longer waiting times increase patient morbidity, TAVI complication rates and mortality. In one study, the cumulative probability of mortality while waiting reached 4.3 % and heart failure-related hospitalisations 14.7 % (19). Despite TAVI developments, a significant increase in waitlist mortality from 2012 to 2018, corresponding to 2.3 % and 5.2 % (20), was established. Associated hazards of the prolonged waiting times do not end with TAVI execution: a relative increase in 1-year postprocedural mortality was observed by 2 % per week

spent on the waitlist (21). A functional decline is a known characteristic of waiting time (22), which in turn might lead to needing an urgent TAVI that predetermines worse outcomes than elective. According to a study, 20 % of waitlisted candidates underwent nonelective hospitalisation with urgent TAVI (23). From a health economics perspective, longer waiting times are associated with loss of quality-adjusted life years and shortening waiting times would indeed be cost-effective (24).

Considering the substantial implications of prolonged waiting times, the primary aim of this study was to evaluate the dynamics of TAVI waiting times from 2009 to 2024 in Vilnius University Hospital Santaros Klinikos (VUH SK) and possible predictors of waiting times. The following objectives were set:

1) to define sociodemographic and baseline health characteristics of the TAVI-receiving patient population in 2009 – 2024;
2) to determine TAVI waiting times from 2009 to 2024 and examine differences in sociodemographic and health condition characteristics during contemporary 2021 – 2024 TAVI practices;
3) to identify factors associated with shorter or longer waiting times in 2021 – 2024.

4. LITERATURE REVIEW

4.1. Methods and Overview

Literature review was performed using the National Library of Medicine PubMed database with the following keywords and their combinations: TAVR and Waiting time, TAVI and Waiting time, TAVR and Delay time, TAVI and Delay time. Article inclusion criteria were: i) published between 2014 and 2024; ii) estimated TAVI waiting time from real-life quantitative research data. In total, 17 articles were reviewed; their characteristics are described in Table 1.

TAVI waiting time research is expanding with each year. At the beginning of the review period in 2014, there was scarce data on TAVI waiting times. One study from 2014 stated that their research was the first to assess the consequences of prolonged waiting times (25), and most of the articles included were published in the second half of the decade. Most studies came from Canadian TAVI registries (41.17 %, n = 7) and in total, data on waiting times were published from 9 countries. Study designs were highly variable – 11 (64.71 %) studies were retrospective cohorts, 4 (23,53 %) studies provided 3-date-point calculations supplementing total waiting time calculations with intermediate times, 3 studies compared TAVI and SAVR waiting times, one study included comparisons between countries (France, United Kingdom (UK), Germany). Sample size and timing varied as well. The largest sample size was 11,077 (of which 6,668 received TAVI) (26), and the smallest was 32 cases (22). In total, 2008 – 2023 TAVI recipient waiting times were represented, with

the longest study span being 11 years (2012 – 2023) (27). A lack of reliable data points was common among exclusion criteria, and only one study pointed out urgency (23). The way of reporting the waiting time differed, even though most of the studies provided median estimates, 6 (35.29 %) studies reported only means, making inter-comparisons difficult. The lowest total waiting time median was 18.3 days in the French IMPULSE trial cohort (28), and the highest was 235 days in the Spanish VH Cohort (24).

Additional sources for estimations of waiting time are available. Valve for Life initiative published data on 23 UK centres during 2019, where the total waiting time from referral to TAVI was a median of 141 days (interquartile range from 115 to 165); additional time points included referral, clinic appointments, and multidisciplinary team (MDT) meetings. A 2022 European survey of TAVI operators (29) did not provide exact numbers, but it was established that TAVI waiting time was below 2 months in 58 % of involved centres, the largest number of centres whose waiting time spanned more than 6 months was located in the Eastern Europe region (to which Lithuania was assigned) with 18 centres.

Table 1. Summary of Publications Included in Literature Review

Year	**First Author**	**Type of Study**	**Country**	**Sample size[1] (year included)**	**Registry**	**Waiting time, days[2]**
2014	Malaisrie et al. (30)	Retrospective cohort	USA	823 (2008 – 2012)	-	2.9[3] (1.3–5.1) weeks
2015	Forman et al. (22)	Prospective cohort	Canada	32 (2012 – 2013)	-	55 (13 – 307) 69^{M} (±62)
2018	Elbaz-Greener et al. (19)	Retrospective cohort	Canada	2231 (2010 – 2016)	CorHealth	105 (53 – 174) 131^{M} (±116.8)
2018	Ribera et al. (24)	Cost-effectiveness analysis	Spain	152 (2008 – 2014)	VH Cohort, TEVAS	235 (124 – 427) 309^{M} (±275)
2019	Elbaz-Greener et al. (23)	Retrospective cohort	Canada	2170 (2010 – 2016)	CorHealth	107 (55 – 176) 132.5^{M} (±117.4)
2019	González Saldivar et al. (31)	Prospective cohort	Spain	59 (2014)	IDEAS	2.9^{M} (±1.6) months
2020	Albassam et al. (32)	Retrospective cohort	Canada	3998 (2012 – 2018)	CorHealth	84 116^{M}
2020	Henning et al. (20)	Retrospective cohort	Canada	3894 (2012 – 2018)	CorHealth	99 – 137.5[4]
2020	Lutz et al. (28)	Prospective cohort	Germany, UK, France	2052 (2015 – 2018)	IMPULSE, IMPULSE enhanced	$22.7^{M, DE}$ (±25.1) $18.3^{M, FR}$ (±19.9) $43.1^{M, UK}$ (±26.9)

Table 1. Summary of Publications Included in Literature Review (continued)

2020	Wijeysundera et al. (33)	Retrospective cohort	Canada	4861 (2014 – 2017)	-	107 – 135[4]
2022	Roule et al. (21)	Retrospective cohort	France	383 (2013 – 2019)	FRANCE-TAVI, FRANCE-2	144.2[M] (± 83.87)
2023	Hewitson et al. (34)	Retrospective comparative	UK	227 (2020 – 2021)	-	93[M]
2023	Ryffel et al. (35)	Prospective cohort	Switzerland	1069 (2019 – 2021)	Bern TAVI	74.41[M] (±91.40)
2023	Stehli et al. (36)	Prospective cohort	Australia	407 (2018 – 2021)	ACE	148 (94–206)
2024	Nilsson et al. (37)	Retrospective cohort	Sweden	7280 (2008 – 2020)	SWENTRY	53
2024	Zaheer et al. (26)	Retrospective cohort	Canada	6668 (2018 – 2022)	CorHealth	67 (28 – 122), 90[M]
2024	Tupa et al. (27)	Retrospective cohort	USA	1565 (2012 – 2023)	-	14 – 43 (7-74.5)[4]

[1] Actual number of TAVI cases, in some cases extracted from the total sample, from which median and/or mean waiting times were estimated (except for *Malaiserie et al. (2014)*).
[2] Waiting time is provided as medians of days if not noted otherwise in the cell. Q1 and Q3 or SD are noted in the brackets; if not, the authors did not provide these parameters.
[3] Waiting times were provided for the combined SAVR and TAVI cohort
[M] Provided estimate is mean, not median.
[4] The total generalised waiting time of all TAVI temporal groups was not provided.
[DE] Germany, [FR] France, [UK] United Kingdom.

4.2. Definitions of Waiting Time

The definitions of time points for waiting time calculations were heterogeneous and, in some cases, vague. It is to be expected as different healthcare policies and sociodemographic situations imply significant differences in patient pathways to TAVI within each country; registries are oftentimes more focused on procedural and postprocedural outcomes, not on the processes that led to the procedure (38). A referral was the most commonly mentioned date point for initiating the waiting time count (41.18 %, n = 7) or as the intermediate point (5.88 %, n = 1). However, it is not entirely clear what a referral encompasses and its timing in relation to the TAVI cardiological evaluation – it might be a referral to a specialized clinic for further evaluations regarding TAVI or already, after the completion of all the necessary evaluations, a referral to the Heart team or straight to the TAVI waitlist. 5 studies did not detalize, what a referral meant in their particular case. Of those referrals that were more detailed, 2 were directed towards the aortic valve replacement (AVR) team (32,33) – one can presume that the evaluation was already completed, 2 to the hospital (21,36) – evaluation could have followed later on, and referral in one study was the second date point (following diagnosis time point) (35), this could indicate a referral for MDT. MDT meeting was another standard variable in 4 studies (19,24,34,36), in one publication representing the first point of the calculation (24). For

the first point, the date of transthoracic echocardiography (TTE) diagnosis was selected by 2 studies (31,34), the decision to intervene was included in 2 studies (31,37), and one study provided two dates – coronary angiogram and computed tomography angiography (CTA), resulting in two waiting times (27), both a recommendation for AVR (30) and TAVI eligibility assessment (22) were utilized once. 4 studies had a second–intermediate date point, of which 3 were MDT and 1 was the aforementioned referral. 10 studies extended after the TAVI date and included mortality and complications data. This follow-up spanned 30 days to 1 year after TAVI or the end of the study observation period.

4.3. Factors Influencing Waiting Time

Multiple studies examined which factors determine waiting time (19,20,23,26,31–33,36). The associations can be categorised into three main categories: healthcare as a system-related, patient clinical status, sociodemographic and patient health status-related.

4.4. Healthcare System Related

TAVI funding had a remarkable toll on the waiting times – a study from Canada (19) captured a significant 63 % (median shift from 322 to 118 days) decrease in waiting times comparing the pre-reform period and the newly established provincial TAVI funding period. However, the following 3 years after the reform, waiting times did not decline significantly and stabilised (19). Another Canadian registry-based study (33) determined that referral year explained 35 % of the variation in waiting times in 2014. TAVI before 2017 (between 2012 and 2016) determined shorter waiting times (32). The same study compared TAVI and SAVR waiting times and identified that even being referred for TAVI predicted longer waiting times (32). The COVID-19 pandemic also contributed to globally reduced TAVI volumes (39); consequently, one study identified a significant increase in waiting time during the surge period (35).

A meta-analysis in 2018 estimated that with the expansion of indications to low-risk, the number of potential annual TAVI candidates in Lithuania would increase from 655 to 1009 cases (40). In 2018, VUH SK served approximately 44.8 % of the Lithuanian population of 65 years old or over (41); therefore, the potential number of VUH SK TAVI candidates should have been between 293 and 452 in 2018. Considering the yearly increase in the proportion of the elderly population, contemporary prevalence of TAVI candidates should be even higher.

4.5. Sociodemographic

As TAVI is a highly complex procedure requiring advanced resources and particular preparation, access issues related to socioeconomic and demographic backgrounds are likely. A 48 % difference in waiting times was determined between Canadian provinces (33). Counterintuitively, another Canadian study found that inhabitants of rural areas had shorter waiting times (19).

Additionally, a Swedish study reported no significant regional differences between administrative units with or without local TAVI centres (37).

Female sex was associated with longer wait times in 3 studies (32,33,36), and a complex relationship between sex and comorbidity burden was established (36), with comorbidities resulting in prolonged waiting times in women but not in men. Henning et al. (2020) (20) demonstrated the lowest income quintile association with longer waiting times. Another study analysed the impact of insurance type and determined that public insurance had longer work-up waiting times compared to private (36). Ethnic concentration was positively related to the length of waiting time – the more diverse the community, the longer the waiting times were registered (26).

4.6. Health Status-Related

Patient health-related factors driving shorter waiting times were urgent TAVI, valve-in-valve interventions (19) and previous cardiac procedures (such as percutaneous coronary interventions, coronary artery bypass graft, SAVR) (20), heart failure (19,20), and ischaemic heart disease (20). A study(31) that categorised waiting times as shorter or longer than 2 months established that waiting times below 2 months were more likely in patients with left ventricular hypertrophy and angina at rest. Alternatively, longer waiting times were predisposed by more expressed comorbidities (32), chronic obstructive pulmonary disease in 2 studies (19,20) and frailty in 3 studies (19,20,32).

Associations with age across studies were inconsistent. Three studies connected increased age with shorter waiting times (19,31,32). In contrast, older age as a factor for longer waiting times was shown in two studies (33,36).

4.7. A Search for an Optimal TAVI Waiting Time Threshold

To date, no universal time duration has been agreed upon for TAVI work-up and implantation. A couple of studies examined waiting time and its relation to post-procedural outcomes, some of which examined waitlist events. A study using mathematical simulation modelling on PARTNER A and PARTNER B data (25) established an increased probability of not meeting noninferiority to SAVR in the PARTNER A trial when TAVI waiting times exceeded 60 days.

British Cardiovascular Intervention Society (BCIS) has set a target of 18 weeks as a maximum waiting time from referral to TAVI (42) and has dedicated equally 6 weeks to the following steps of the patient pathway: i) referral to clinic and necessary investigations for MDT discussion, ii) from decision to TAVI. The Valve for Life (43) project in the United Kingdom presented an even more ambitious goal: 8 weeks from referral to definitive treatment of AS by TAVI or SAVR (44).

The Canadian Cardiovascular Society released a statement in 2019 with recommended waiting times: 12 or fewer weeks for the elective patient group, 2 or fewer for the urgent and 48 or

fewer hours for the emergent group (45). The Canadian research group that published all Canada-related articles included in this review published simulation-based waiting time benchmarks for TAVI (46) depending on risk stratified by the CAN3T (47) instrument, created to predict the patient risk of experiencing adverse events during waiting time. They proposed 3 weeks from referral to TAVI for high-risk patients, 7 weeks for medium-risk patients, and 16 weeks for low-risk patients(46). Target: Aortic Stenosis, an initiative by the American Heart Association, has set quality measures as the percentage of patients with a class I indication that undergo AVR in 90 days following AS diagnosis and 30 days following MDT evaluation (38).

There is substantial evidence of the detrimental effects and potential causes of prolonged TAVI waiting times. However, the data originate from 9 Western, high-income countries, yet the findings noticeably differ across studies. This supports the continuation of research on waiting times, especially in previously unexplored regions. With expanding TAVI indications and increasing demand, it is essential to continue the development of TAVI waiting time research to further optimise clinical pathways and adapt to increasing caseloads. No previous research in this field was identified in Lithuania or sociodemographically similar Baltic or Eastern European countries. Therefore, it is essential to pursue this topic to address the knowledge gap on the situation in Lithuania, as it might differ from previously discussed regions.

5. METHODS

5.1. Sample Formation and Variables of Interest

The design of the study was a single tertiary centre retrospective observational analysis of the waiting times for the TAVI intervention between 2009 and 2024 in VUL SK. The data source for the study was the medical records of the digital patient history of the VUL SK, and approval from the regional ethics committee (No. 2025/2-1626-1090) was obtained. In total, 866 TAVIs were performed in the research centre during the study period. Inclusion criteria were the following:

1) TAVI was performed in the research centre;
2) ultrasound-confirmed diagnosis of severe aortic valve stenosis before TAVI;
3) clear data points for the outcome variables.

For exclusion criteria, previous balloon aortic valvuloplasty (BAV) was selected, as this group often had an unusual pathway to TAVI, and it was problematic to identify the exact time points for waiting time calculations. As a result, 60 cases were excluded: 34 cases had previously undergone BAV, 25 cases lacked reliable dates, and for 1 case, third-grade valve insufficiency was the indication of the

procedure. Of the excluded cases, 36 were performed in 2009 – 2020 and 24 in 2021 – 2024. As a result, 806 cases comprised the sample for this study (Figure 1).

Outcome variables and relevant time points were selected based on current literature and the accessibility of particular information in the research centre's digital system, enabling the extraction of the identical date for as many cases as possible. The date of referral was one of the most frequently reported variables in TAVI waiting time studies, though it was often diversely defined. The first date point of this study – an appointment in VUH SK when severe AS was confirmed by ultrasound and an indication for aortic valve replacement was documented – could be considered a form of referral to the hospital, diagnosis and TTE date, previously used in four other waiting time publications (Section 4.2). For the middle date point between the beginning of the TAVI pathway and TAVI itself, the date of the last standard cardiological evaluation was chosen, as all patients receive computed tomography angiography (CTA) in the research centre and, frequently, coronary angiography as well and if not, it was always well documented in the hospitalisation records. As a result, the primary outcome variable was total waiting time (TWT) – time in days from the indication of TAVI to the date of TAVI. Secondary outcome variables were: 1) procedural waiting time (PWT) – time in days from the date of the last evaluation test to the date of TAVI; 2) evaluation waiting time (EWT) – time in days from the indication date for AVR to the last part of the standard cardiological evaluation – CTA or coronary angiography, whichever happened later.

Valve Academic Research Consortium 3 definitions were reviewed (48). Variables related to preprocedural health status were documented (Table 3). Urgency was categorised as elective or non-elective. Non-elective TAVI was defined as TAVI performed during a non-elective hospitalisation, expedited elective TAVI following initial diagnosis during a non-elective hospitalisation, or TAVI initially planned as elective but expedited due to cardiac deterioration requiring non-elective hospitalisation. Other independent variables were chosen to define patient sociodemographics: age, sex, and type of residence, such as city, urban or rural area, Vilnius or non-Vilnius. Additionally, any documented reasons for TAVI delays were noted. Supplemental data were requested from the National Health Insurance Fund on governmental TAVI funding and the VUH SK Radiology department on annual volumes of CTA under TAVI protocol.

5.2. Descriptive and Inferential Analysis

Exploratory data analysis was performed using Microsoft Excel (Microsoft 365 MSO), IBM SPSS (version 30.0) and R (version 4.4.3.) software. Outcome variables were tested for normality using simple histograms that presented right-skewed, leptokurtic distributions with apparent outliers, and the Shapiro-Wilk test confirmed statistically significant differences from the Gaussian distribution. Therefore, medians (Mdn) were chosen to describe the central tendencies due to their

robustness against skewness. They were reported along with the 25th (Q1) and 75th (Q3) percentiles in brackets (Q1; Q3). In the descriptive tables, interquartile ranges (IQR), means (M), and standard deviations (SD or ±) were additionally provided.

Only cases between 2021 and 2024 were included for inferential analyses to capture the most recent relevant situation. It is established that higher TAVI centre volume yields lower mortality and complication rates (49), and even though ESC has not established any specific volume requirements, USA structural heart specialist organisations in 2018 have set a 50 cases per year threshold for TAVI programmes to be certified (50). It could be considered that TAVI in Lithuania during 2009 – 2019 was in its developmental phase: governmental funding decreased between 2012 and 2017, and a substantial financial injection was made only at the end of 2019; procedural volume each year was below 50. The year 2020 was still transitional in terms of funding and case volume, and it is plausible that the COVID-19 pandemic caused fluctuations in waiting times that are not more relevant nowadays and would distort the picture of regular current clinical practice. Therefore, 2021 was selected as the starting point of the current TAVI practices in VUH SK. Only non-parametric statistical tests were available for analysis. Mann-Whitney U was used to compare distributions between 2 groups, and the Kruskal-Wallis criterion was used to compare 3 or more groups, which, when significant, was followed by a post hoc pairwise comparison with Bonferroni significance correction. A Spearman's rank correlation test was performed between variables with quantitative alternatives (TWT, age, body mass index, pulmonary artery pressure (PAPS)). Associations between categorical variables were analysed using the Pearson Chi-square test. If the expected cell counts were less than 5, the Fisher-Freeman-Halton Exact (Exact for further reference) test for larger than 2x2 tables was utilised. For identifying pairs of groups with significant differences, a post hoc Z-test with Bonferroni correction was applied. Statistically significantly different groups were indicated by different letters in the cell values. In addition, effect sizes and their confidence intervals were provided for all statistical tests. The selection of effect measures and interpretation is provided in Table 2.

Table 2. Selected Effect Size Parameters and Their Interpretation Levels

Parameter (abbreviation)	**Statistical test**	**Small**	**Medium**	**Large**
Eta-squared H (η^2_H) (51)	Kruskal-Wallis	0.01	0.06	0.14
Common language effect size (CLES) (51)	Mann-Whitney U	0.56	0.65	0.75
Cramer's V (V) (52,53)	Chi-square	2 Cat. = 0.10 3 Cat. = 0.07 4 Cat. = 0.06	2 Cat. = 0.3 3 Cat. = 0.21 4 Cat. = 0.17	2 Cat. = 0.5 3 Cat. = 0.35 4 Cat. = 0.29

Cat. – is an abbreviation for category and corresponds to the number of categories of the variables included in the contingency table. The variable with fewer categories is chosen for effect size interpretation (52).

Cox models were the most often used in TAVI waiting time analysis (19–21,23,26,30,32,33,35); however, censored cases are necessary for this modelling, and by the present study design, no cases remained on the waitlist. Therefore, a logistic regression model (LR) was selected, as it was previously applied in TAVI waiting time publications (21,30,31), odds ratios are comparably understandable and interpretable in the clinical setting, and all logistic regression assumptions were satisfied (54). A dichotomous dependent variable was created by categorising TWT according to its median value – median and below the median (0) or above the median (1). A two-sided P-value below 0.05 was considered statistically significant.

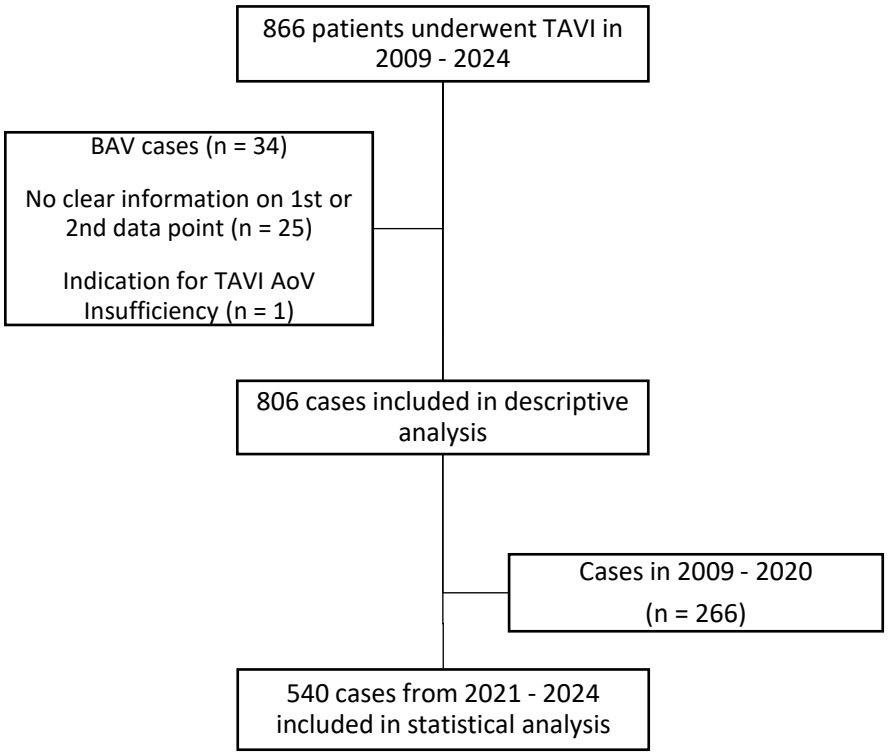


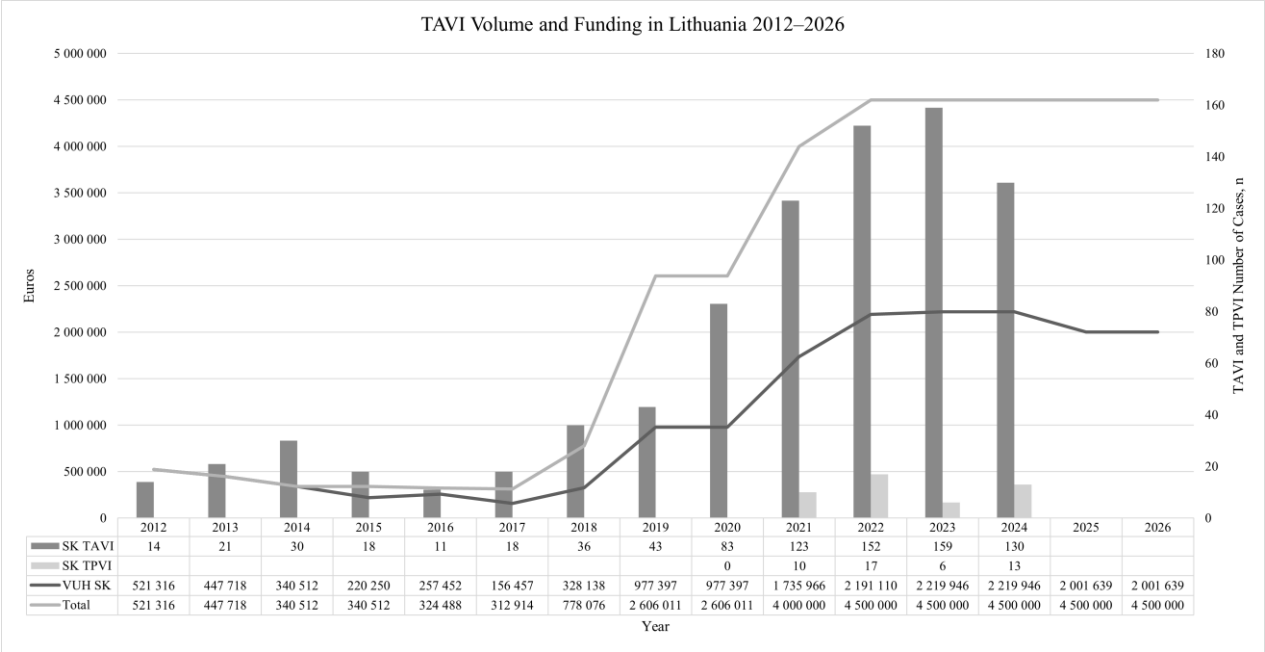
Figure 1. Flowchart of study sample formation

6. RESULTS

6.1. Overview of TAVI Volume in the Centre

From 2009 until 2024, TAVI's annual case volume has steadily increased, except for 2015 and 2016, when annual volumes dropped (18 and 11 cases, respectively). The steepest increase was captured between 2019 and 2021, surging from 43 to 123 cases in 2 years. However, in 2024, a remarkable decrease was observed, reducing the caseload to the 2021 level. The exact number of cases performed in VUH SK and dedicated funding in 2012 – 2024 is presented in Figure 2, and the

exact number of annual cases included in the study is presented in Supplementary Materials, Figure 11.



	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026
SK TAVI	14	21	30	18	11	18	36	43	83	123	152	159	130		
SK TPVI									0	10	17	6	13		
VUH SK	521 316	447 718	340 512	220 250	257 452	156 457	328 138	977 397	977 397	1 735 966	2 191 110	2 219 946	2 219 946	2 001 639	2 001 639
Total	521 316	447 718	340 512	340 512	324 488	312 914	778 076	2 606 011	2 606 011	4 000 000	4 500 000	4 500 000	4 500 000	4 500 000	4 500 000

Figure 2. VUH SK TAVI volume in 2012 – 2024, VUH SK TPVI volume in 2020 – 2024, TAVI and TPVI funding in VUH SK and Lithuania in 2012–2026.
Note: Information on funding was available from 2012 onwards. From 2015, funding was allocated to the TAVI centre in Kaunas and from 2017 in Klaipėda. Since 2023, funding has been appointed for 2-year periods, and though total TAVI funding in 2022 – 2026 remained unchanged, funds for the VUH SK TAVI programme were reduced for 2025 – 2026. Throughout the period, funding was allocated for TAVI and Transcatheter pulmonary valve implantation (TPVI) together; to date, TPVI in Lithuania has only been performed in VUH SK. TPVI volumes in 2020 – 2024 were obtained from National Health Insurance Fund public reports (55). TAVI and TPVI volumes here are provided as a number of patients treated and not valves used, meaning a few patients could have required a second transcatheter heart valve during the index procedure, and that was not reflected in the graph.

Overall, VUH SK TAVI case volume did not entirely correspond to TAVI funding trends. Governmental funding since its establishment in 2012 until 2017 decreased, but TAVI volume and evaluation load progressed, with CTAs surpassing 50 in 2015, 100 in 2018, and 200 in 2022 (Figure 3). In 2022, 103 more CTAs than TAVIs were performed; in 2023 and 2024, the difference decreased to 81 and 97 cases, respectively. Funding in 2021 – 2024 remained stable, but the TAVI volume and CTA numbers showed a declining trend.

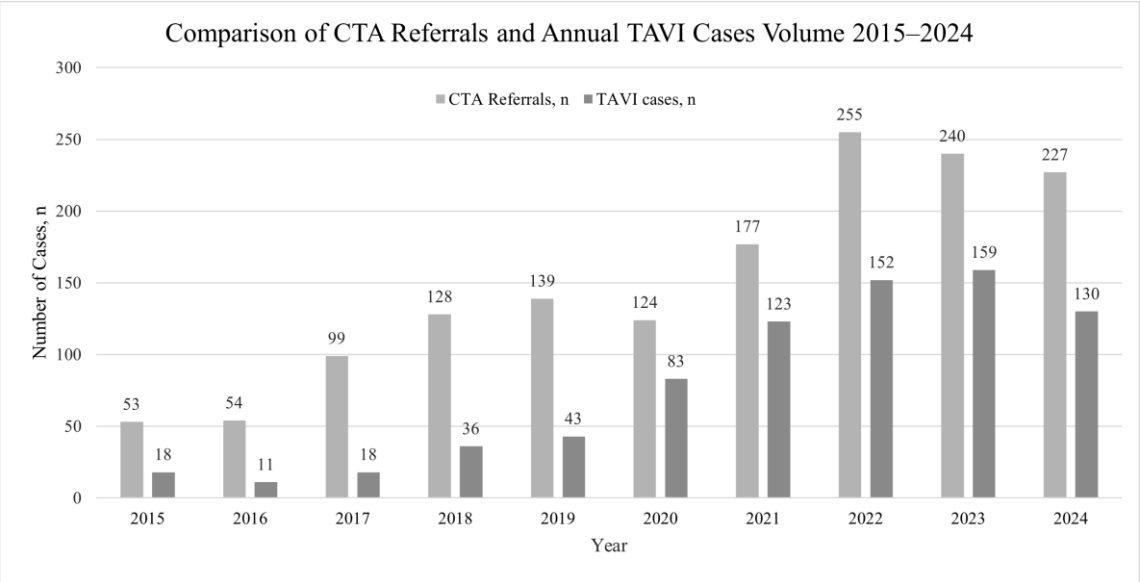


Figure 3. Annual CTA Referrals and TAVI Cases Volume

6.2. Sociodemographic characteristics in 2009 – 2024

The median age of the sample was 80 years (77; 83), and the mean was 79.88 years (± 5.81). According to the ESC 2021 guidelines (5), one of the criteria guiding the choice of TAVI versus SAVR is age 75 or older, favouring TAVI. Therefore, the age variable was split into two categories for additional analysis: those under 75 years old, who comprised 14.64 % (n = 118) of the sample, and those 75 years old and older (85.36 %; n = 688). As seen in Figure 4A, the tendency of most patients to be 75 years or older was consistent throughout the year. In 2016 and 2017, all TAVI cases were performed in patients 75 or older, but in 2012, the younger patient group comprised almost one-third of all the cases.

In total, more women (64.89 %, n = 523) received TAVI in 2009 – 2024, with the most notable relative differences in sex distribution appearing during the first year, 2016 and 2017 – 60 %, 71.4 % and 46.6 %, respectively (Figure 4B).

From 2009 to 2024, 51.36 % (n = 414) of patients were from Vilnius. In the second and third years of TAVI in VUL SK, most patients lived outside Vilnius city, 80 % (n = 8) and 75 % (n = 9), respectively. Later, the proportions stabilised, with the largest differences observed in 2017 (28 % difference), 2020 (16 % difference) and 2016 (14 % difference) (Figure 4C).

More detailed place of residence analysis showed that there were 56.58 % (n = 456) patients from cities, 21.96 % (n = 177) from rural areas and 21.46 % (n = 173) from urban areas. From 2012, most of the patients were from larger cities, which is not unexpected, considering that Vilnius residents generally comprised half of the patients. In 2010 and 2011, the largest (40 % (n = 4) and 50 % (n = 6), respectively), and from 2012 to 2017, the second largest proportion of the patients lived in rural areas. That changed in 2018, when more urban area residents received TAVI compared to rural

residents, 30 % (n = 9) and 13 % (n = 4), respectively. Since 2020, the proportions have fluctuated but stayed comparably similar (Figure 4D).

Figure 4. Distributions of the Study Sample by Age (A), Sex (B), City of Residence (C) and Residence Size (D)

6.3. Baseline health characteristics

Heart failure was confirmed for almost all cases; only three lacked such a record. The most common comorbidities among the VUH SK TAVI patient population were arterial hypertension (95.91 %, n = 773) and dyslipidemia (80.65 %, n = 650). The complete prevalence of comorbidities is summarised in Table 3.

Table 3. Prevalence of comorbidities among the sample

Comorbidity		**n (%)**	
Arterial hypertension		773 (95.91)	
Dyslipidaemia		650 (80.65)	
NYHA classification (56)	I class	11 (2.06)	
	II class	145 (27.15)	
	III class	362 (67.79)	
	IV class	16 (3)	
Left ventricular ejection fraction (LVEF) (%)	Below 30	21 (3.89)	
	30-40	54 (10)	
	41-49	31 (5.74)	
	50 or above	433 (80.19)	
Risk groups, according to EuroSCORE II (57) estimates	Low	339 (62.78)	
	Intermediate	135 (25)	
	High	66 (12.22)	
Chronic kidney disease	Chronic kidney disease	303 (37.59)	309 (38.34)
	Dialysis	5 (0.62)	
	Kidney transplant	1 (0.12)	
Atrial fibrillation or flutter	Permanent	107 (13.28)	297 (36.84)
	Long-standing persistent (>12 months)	8 (0.99)	
	Persistent (>7 days)	59 (7.32)	
	Paroxysmal (<7 days)	123 (15.26)	
Diabetes mellitus	Type 2	186 (23.11)	189 (23.45)
	Type 1	3 (0.37)	
Diabetes mellitus treatment	Oral antidiabetics	118 (14.64)	161 (19.98)
	Insulin	19 (2.36)	
	Multiple medications	14 (1.74)	
	Diet	10 (1.24)	
	>12 months	93 (11.54)	

Table 3. Prevalence of comorbidities among the sample (continued)

Previous myocardial infarction (MI)	3-12 months	28 (3.47)	154 (19.11)
	<3 months	30 (3.72)	
	Yes (unspecified)	3 (0.37)	
Peripheral arterial disease		125 (15.53)	
Previous cerebrovascular incidence	Stroke - unclassified	38 (4.71)	82 (10.17)
	Stroke - persistent dysfunction	27 (3.35)	
	Stroke - full restitution	4 (0.5)	
	TIA	13 (1.61)	
Chronic obstructive pulmonary disease (COPD)	Chronic obstructive pulmonary disease or emphysema	35 (4.34)	84 (10.42)
	Asthma	29 (3.6)	
	Other or a combination of both previous categories	20 (2.48)	
Liver disease	Cirrhosis	6 (0.74)	12 (1.49)
	Other	6 (0.74)	
Cancer		74 (9.19)	
Immunosuppression		8 (0.99)	

The median value of EuroSCORE II was 3.075 (1.88; 5.03; IQR = 3.16), and the mean was 4.31 (±4.048). The median body mass index was 28.48 kg/m^2 (25.34; 32.29; IQR = 6.95). The systolic pulmonary artery pressure median was 41 mmHg (33; 54; IQR = 21).

A significant amount of the sample had previously undergone cardiac interventions. Electrophysiological interventions (pacemaker, cardioverter-defibrillator or cardiac resynchronisation therapy) were applied in 14.39 % (n = 116) cases. 2.73 % (n = 22) of cases had previously undergone valvular surgery, of which 81.82 % (n = 18) were aortic valve-related: SAVR, Bantall De Bono or Ross procedures. 30.69 % (n = 263) of patients had percutaneous coronary intervention, and 11.09 % (n = 95) had coronary artery bypass graft surgery.

6.4. Waiting Times and their Temporal Trends 2009 – 2024

The median total waiting time was 189.5 days, the median procedural waiting time (PWT) was 78.5 days, and the evaluation waiting time (EWT) median was 62.5 days. Inconsistent differences between central EWT and PWT characteristics and higher interquartile range and standard deviation values of EWT suggest higher variability of the evaluation duration (Figure 5).

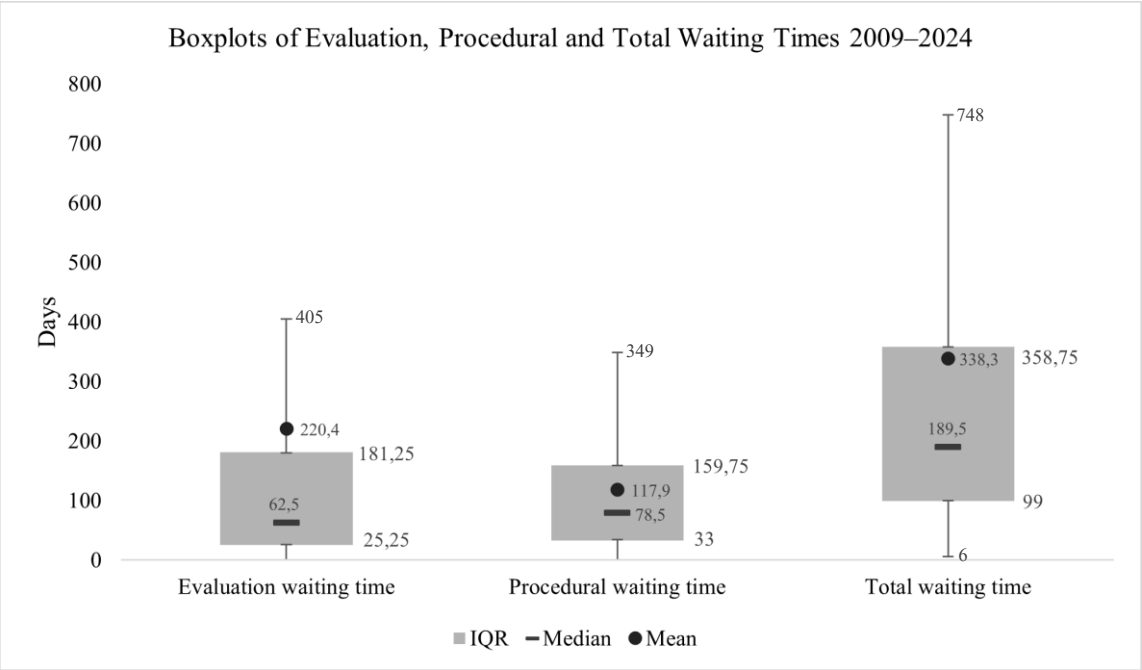


Figure 5. Distributions of evaluation, procedural and total waiting times (2009 – 2024) (calculated using the Tukey method)

The largest medians of total waiting time were 409 days in 2016 (349; 592; IQR = 243) and 390 days in 2012 (246; 790; IQR = 544). Alternatively, the smallest waiting medians were 65 days in 2010 (28.5; 158.75; IQR = 130.25), 153 days in 2022 (89.25; 245; IQR = 155.75), and 155.5 days in 2023 (104; 296.5; IQR = 192.5). However, in 2024, there was a remarkable surge of 82.5 days, resulting in a median of 238 days (104; 377; IQR = 266) (Figure 6). In 2012, a governmental funding regulation was launched; however, it did not trigger a decrease in total waiting time.

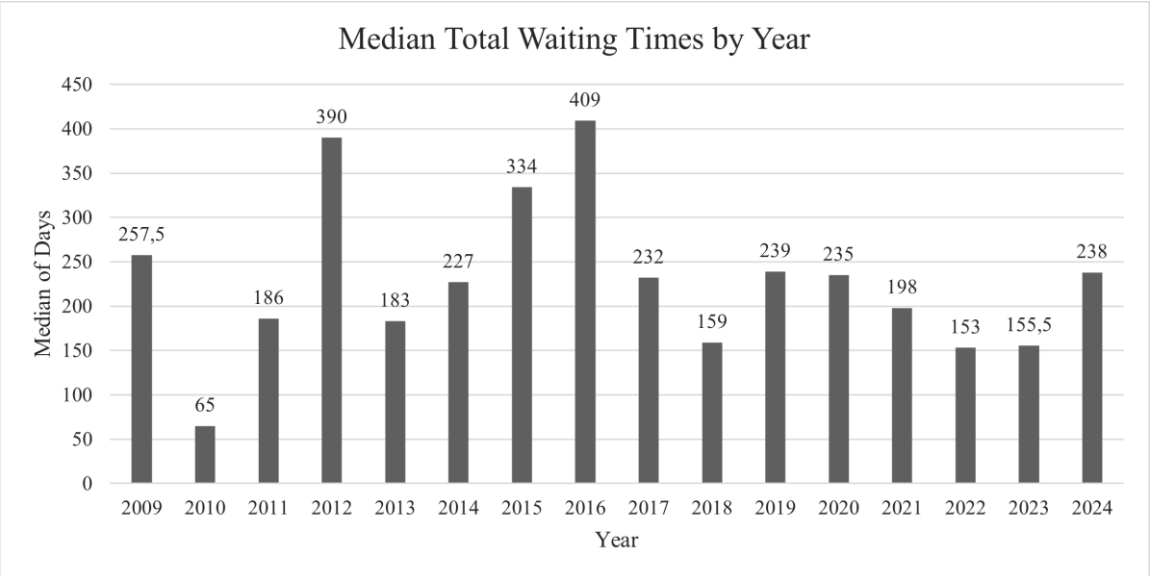


Figure 6. Medians of Total Waiting Time by Year in 2009 – 2024

Median calculations of evaluation and procedural waiting times across 2009 and 2024 are presented in Figure 7. Throughout the year, procedural waiting time duration tended to increase, with peaks in 2016 – 215 days (145; 346.5; IQR = 201.5) and 2024 – 148 days (35; 225; IQR = 190). TAVI volume in 2016 was one of the lowest, only 11 cases, including the ones that did not fulfil study inclusion criteria. From 2020, PWT increased, with the highest difference being 55 days between 2023 and 2024. Median evaluation waiting time was exceptionally long in 2012 – 345 days (77; Q3 = 703; IQR = 626), and the next closest duration – 176 days – was observed in 2016 (73; 280; IQR = 207). Since 2022, the duration has not exceeded the 50-day threshold. Until 2021, median evaluation waiting time was longer than procedural waiting time (except for 2016), but in 2021, evaluation waiting time became shorter and remained so until the end of the study period.

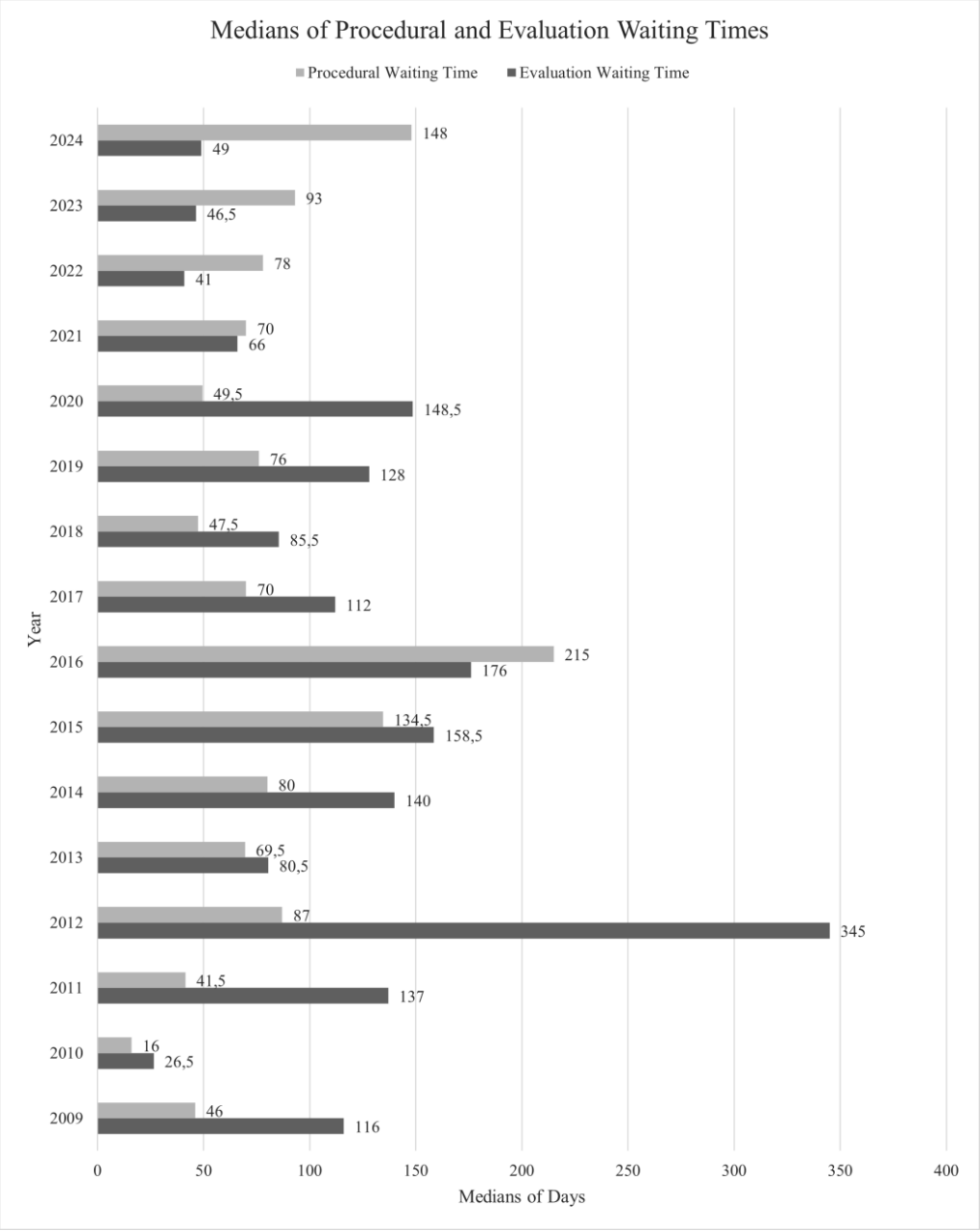


Figure 7. Medians of procedural and evaluation waiting times

6.5. Total Waiting Times between 2021 and 2024

The total waiting time in 2021 – 2024 was a median of 173 and a mean of 305.45 days (Figure 8). The median difference of EWT and PWT (49 and 89.5, respectively) became more pronounced compared to the total sample of 2009 – 2024 (Figure 5).

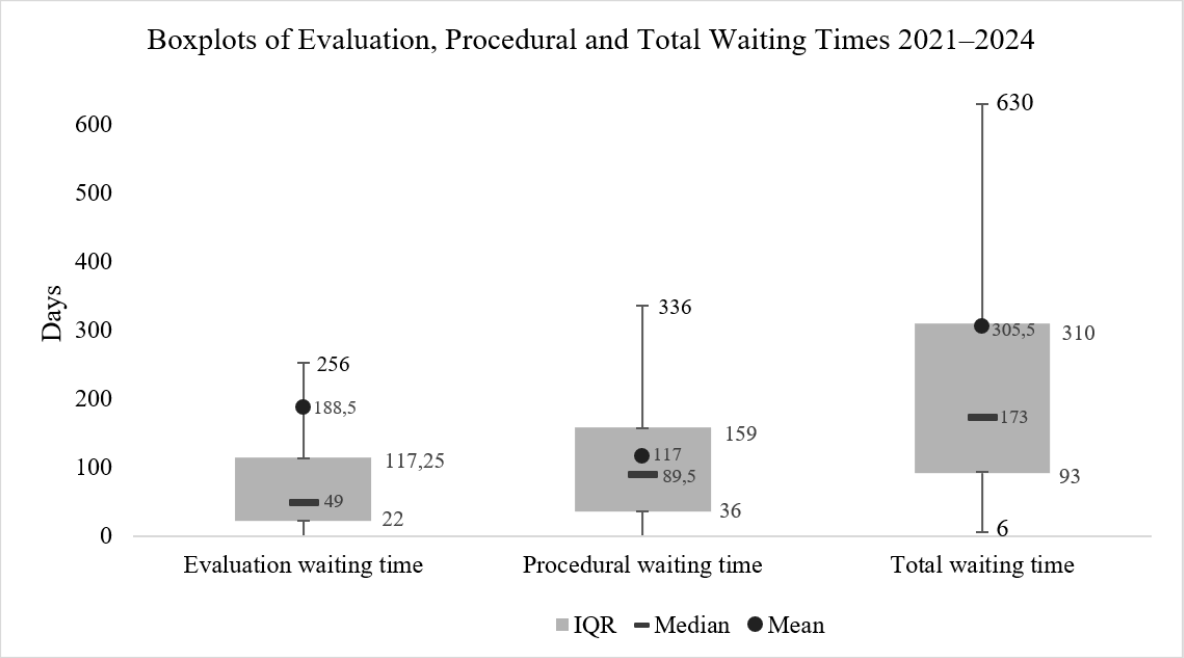


Figure 8. Distributions of evaluation, procedural and total waiting times (2021 – 2024) (calculated using the Tukey method)

6.6. Temporal Differences of Waiting Times, Baseline and Sociodemographic Characteristics.

All waiting times differed significantly across the years. Total waiting time distributions across 2021 – 2024 statistically significantly differed (Kruskal-Wallis test, χ^2 (3, n = 540) = 8.033, p = 0.045, η^2_H = 0.009). Pairwise comparisons revealed that TAVI total waiting times differed significantly between 2022 (153 days) and 2024 (238 days) (p = 0.046). Evaluation waiting time during 2021 – 2024 declined (Kruskal-Wallis test, χ^2 (3, n = 540) = 8.498, p = 0.037, η^2_H = 0.01) with significant pairwise comparison between 2021 (66 days) and 2022 (41 days) (p = 0.048). Procedural waiting time during 2021 – 2024 differed significantly as well (Kruskal-Wallis test, χ^2 (3, n = 540) = 17.791, p < 0.001, η^2_H = 0.028). However, procedural waiting tended to increase. As pairwise comparisons indicated, procedural waiting time in 2024 (148 days) was significantly longer than in 2021 (70 days) (p = 0.001), 2022 (78 days) (p = 0.002) and 2023 (93 days) (p = 0.047). Effect sizes measured by eta-squared H were all in the small range. 95 % bootstrap CIs of effect sizes of EWT and PWT comparisons across 2021 – 2024 included zero, indicating that the actual differences might be minimal. Numeric data about central tendencies is provided in Table 4.

Table 4. Central characteristics of total waiting time in days across 2021 – 2024

Waiting Times	Year	Median	Q1	Q3	p-value	Effect size η^2H	CI[1]
Evaluation Waiting Time	**2021***	66	31	220	0.037	0.01	-0.002; 0.05
	2022*	41	22,5	99,5			
	2023	46,5	23	102,5			
	2024	49	11	103			
Procedural Waiting Time	**2021***	70	26	148	<0.001	0.028	0.006; 0.07
	2022**	78	37	120,75			
	2023***	93	47,5	132,75			
	2024*,,*****	148	35	225			
Total Waiting Time	2021	198	98	336	0.045	0.009	-0.002; 0.04
	2022*	153	89,25	245			
	2023	155,5	104	296,5			
	2024*	238	104	370			

* Pairs of variables marked with the same number of asterisks (*) indicate statistically significant Kruskal-Wallis post-hoc pairwise comparisons ($p < 0.05$).

[1] 95 % Confidence interval of effect size η^2H calculated using the percentile bootstrap method with 1000 samples.

Chronic kidney disease prevalence across the year differed significantly, particularly between 2022 (32.2 %, n = 47) and 2024 (49.6 %, n = 62) (Pearson Chi-Square test, $\chi2$ (3, n = 540) = 8.690, p = 0.034, V = 0.13). Dyslipidemia was more prevalent in 2024 (96 %, n = 120) compared to 2021 (84.6 %, n = 99) and 2022 (84.2 %, n = 123) (Pearson Chi-Square test, $\chi2$ (3, n = 540) = 14.531, p = 0.002, V = 0.16). NYHA distributions during the selected period also differed significantly (Exact Chi-Square test, $\chi2$ (9, n = 540) = 24.664, p = 0.002, V = 0.12). There were more NYHA III class patients and fewer NYHA II class patients in 2024 (77.6 %, n = 97 and 18.4 %, n = 23, respectively) compared to 2023 (58.7 %, n = 88 and 36.7 %, n = 55, respectively). Proportions of patients diagnosed with peripheral arterial disease differed significantly across years (Pearson Chi-Square test, $\chi2$ (3, n = 540) = 10.024, p = 0.018, V = 0.14), particularly in 2023 (9.2 %, n = 14) and 2024 (22.4 %, n = 18). Results of all temporal comparisons are provided in Supplementary Materials Table 7.

6.7. Differences in Total Waiting Time across Groups by Baseline and Sociodemographic Characteristics

Total waiting time across different Left ventricular ejection fraction groups differed statistically significantly (Kruskal-Wallis test, $\chi2$ (4, n = 540) = 23.021, p<0.001, η^2_H = 0.036),

particularly the group of left ventricular ejection fraction (LVEF) values below 30 % had shorter waiting time compared to LVEF 30 – 40 % (58 and 143 days, respectively, $p = 0.027$), and LVEF equal or more as 50 % (182 days) ($p < 0.001$). Patients with previous aortic valve surgery had significantly shorter total waiting times, 92 versus 174 days (Mann-Whitney U test, $U = 3057.5$, $z = -2.192$, $p = 0.028$, CLES = 0.656). The non-elective patient group waited shorter (36 days) than the elective group (196.5 days) (Mann-Whitney U test, $U = 8004$, $z = -9.771$, $p < 0.001$, CLES = 0.815). Patients with a history of myocardial infarction had shorter waiting times – 145 versus 182 days (Mann-Whitney U test, $U = 17915.5$, $z = -2.790$, $p = 0.005$, CLES = 0.59). Total waiting time differed significantly between sexes (Mann-Whitney U test, $U = 29397$, $z = -2.435$, $p = 0.015$, CLES = 0.563), with women having a longer total waiting time at a median of 187 days than men (153 days). Common language effect size calculations indicated a medium effect size of comparison by previous aortic valve surgery, translating to a probability of 65.6 % that a patient with previous aortic valve surgery would wait shorter than one without it. A significant effect was calculated for the comparison of waiting times by urgency status, suggesting that 81.5 % of non-elective patients would receive TAVI faster. Other significant tests yielded small effect sizes. All significant and non-significant between-group comparisons are provided in Supplementary Materials Table 8.

Spearman correlation analyses were performed between quantitative variables. Total waiting time had no significant correlation with age ($p = 0.883$, $\rho = -0.024$), BMI ($p = 0.709$, $\rho = 0.029$), and PAPS ($p = 0.084$, $\rho = -0.11$).

6.8. Documented Delays and Predictors of Total Waiting Times

During data gathering, it was aimed to document any possible causes for a prolonged time until TAVI. The following categories were made:

- Personal – all documented refusals, no-shows, indecisiveness or requests for delay due to personal reasons, objective unsuitability for TAVI and refusal for SAVR during the initial consultation.
- Health-related – management of baseline comorbidities, new findings during evaluation, need for additional evaluation, acute illnesses at the time of hospitalisation that prohibited the TAVI execution, and a purposely selected close observation strategy.
- Other – instances when technical issues, healthcare system peculiarities or multiple reasons were documented.
- Unspecified – represents the group of cases when the reason for the delay was not identified.

A specific reason was not documented for most cases (73.15 %; n = 395). Health-related and personal reason groups were similarly prevalent, accounting for 12.59 % (n = 68) and 12.96 % (n =

70) of all cases, respectively (Figure 9). However, if additional procedures were needed, it did not necessarily mean the case was delayed, or waiting was prolonged. As there are no precise guidelines either in Lithuania or internationally, in this research, a delay was considered a longer total waiting time than the median total waiting time between 2021 and 2024, which was 173 days. When adjusting for this delay threshold and analysing only delayed cases, the most common were personal reasons (23.88 %; n = 64), and health-related reasons became less frequent (17.16 %, n = 46). However, no possible reason for a delay was specified for most patients (57.09 % of the adjusted sample, n = 153). For 29 cases (5.37 % of the total non-adjusted sample), there was a possible cause of prolonged waiting documented; however, they fell under the median of 173 days and, for this research, were not considered delayed (Figure 9).

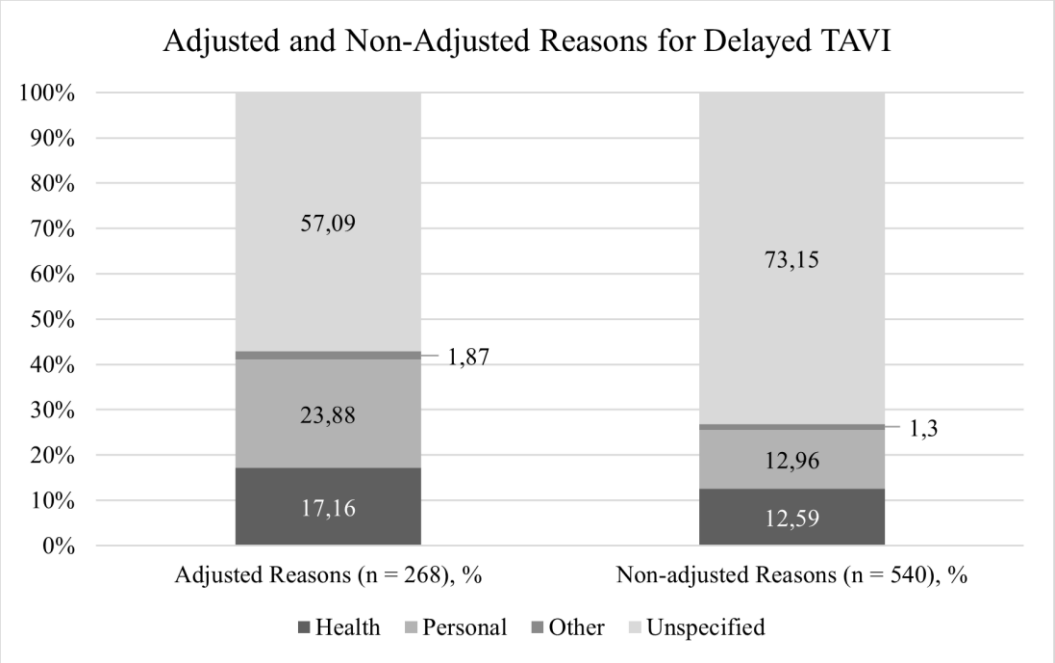


Figure 9. Adjusted and non-adjusted documented reasons for delayed TAVI

Total waiting time across different reason groups differed significantly (Kruskal-Wallis test, $\chi 2$ (4, n = 540) = 423.292, $p < 0.001$, $\eta^2_H = 0.784$) with a considerably large effect size, suggesting 78.4 % of the variance of total waiting time is attributable to reason groups. Pairwise comparisons revealed statistically significant differences between uspecified and personal reasons ($p < 0.001$). Evaluation waiting time differences were significant (Kruskal-Wallis test, $\chi 2$ (4, n = 540) = 240.364, $p < 0.001$, $\eta^2_H = 0.442$), the effect size was again large, indicating 44.2 % explanation of the variance, with statistically significant differences among delayed groups being between unspecified and personal reasons ($p < 0.001$), personal and health reasons ($p = 0.049$). The same pattern was observed in procedural waiting time; it was significantly shorter (Kruskal-Wallis test, $\chi 2$ (4, n = 540) = 172.461, $p < 0.001$, $\eta^2_H = 0.315$) in the personal reasons group compared to the health-related reasons group (p

= 0.014) and compared to unspecified cases (p = 0.018), effect size was smaller corresponding to 31.5 % of the variance though still large. Differences in waiting times between no-delay and other groups are not discussed because the difference is inherent due to the nature of creating a no-delay group consisting of TWT values below the TWT median. However, the procedural waiting time between the no-delay and the other reasons groups did not differ significantly (p = 0.70). Creating a no-delay group could also increase effect sizes; thus, effect sizes and respective confidence intervals were calculated with unadjusted reason groups as the grouping variable and differed at most by 0.003 from those presented in Table 5.

Throughout the year, groups of reasons differed statistically significantly (Exact Chi-Square test, $\chi 2$ (12, n = 540) = 23.097, p = 0.013, V = 0.119); however, the only significant difference was between the proportion of unspecified delays and no delays in 2024. When comparing the compositions of groups by sex, 81.3 % of women comprised the personal reasons group, significantly more than 58.5 % of women in the no delay group (Exact Chi-Square test, $\chi 2$ (4, n = 540) = 12.693, p = 0.009, V = 0.153). There were significantly more cases with previous percutaneous coronary intervention among the health-related delay group compared to other groups (Exact Chi-Square test, $\chi 2$ (4, n = 540) = 29.160, p <0.001, V = 0.232). All effect sizes measured by Cramer's V were small and corresponded to weak associations. The exact proportions are provided in Table 5.

Table 5. Differences in prevalence of adjusted reasons for delay between groups

Variables	Health-related	Personal	Other	Un-specified	No delay	p-value	Effect size	CI
Total Waiting Time	355 (252.75; 524.75)	**699*** (469.25; 1165.25)	706 (380; 1693)	**265* (211; 350.5)**	94.5 (54.25; 141)	<0.001	0.784	0.77; 0.8
Evaluation Waiting Time	**110.5*** (61; 232)	**582*,**** (197.75; 1081)	529 (142; 1601)	**86** (43; 174.5)**	29 (8; 48)	<0.001	0.442	0.38; 0.52
Procedural Waiting Time	**193.5*** (109; 242.75)	**97.5*,**** (36; 193)	117 (45.5; 314.5)	**162** (97.5; 224)**	55 (21.25; 93)	<0.001	0.315	0.25; 0.39
2021	8[a] (17.4)	19[a] (29.7)	1[a] (20)	36[a] (23.5)	53[a] (19.5)	0.013	0.119	0.104; 0.186
2022	13[a] (28.3)	10[a] (15.6)	2[a] (40)	34[a] (22.2)	87[a] (32)			

Table 5. Differences in prevalence of adjusted reasons for delay between groups (continued)

2023	12[a] (26.1)	18[a] (28.1)	1[a] (20)	35[a] (22.9)	86[a] (31.6)			
2024	13[a,b] (28.3)	17[a,b] (26.6)	1[a,b] (20)	**48[b] (31.4)**	**46[a] (16.9)**			
Sex (Female)	31[a, b] (67.4)	**52[a]** (81.3)	4[a, b] (80)	99[a, b] (64.7)	**159[b] (58.5)**	0.009	0.153	0.101; 0.235
Percutaneous coronary intervention	**32[a]** (69.6)	18[b] (28.1)	2[a, b] (40)	45[b] (29.4)	86[b] (31.6)	<0.001	0.232	0.159; 0.324

For quantitative variables, medians, Q1 and Q3 are provided in cells, and the effect size was calculated using the eta squared H method. For categorical variables, count values and percentage of the total column (reason group) are provided in the cells, and the effect size was calculated using Cramer's V.
* Pairs of variables marked with the same number of asterisks (*) indicate statistically significant Kruskal-Wallis post-hoc pairwise comparisons ($p < 0.05$).
[a, b] Statistically significantly different groups according to the Chi-square post hoc Z-test were indicated by letters in the cell values.

Differences between adjusted reasons for delay groups were not significant across age as a quantitative variable ($p = 0.303$), BMI ($p = 0.802$), and PAPS ($p = 0.857$). Proportions of reason groups did not significantly differ between Vilnius and non-Vilnius ($p = 0.910$), settlement size ($p = 0.945$), age groups ($p = 0.323$), LVEF groups ($p = 0.147$), previous myocardial infarction ($p = 0.147$), NYHA groups ($p = 0.453$), peripheral arterial disease ($p = 0.527$), diabetes ($p = 0.338$), COPD groups ($p = 0.795$), arterial hypertension ($p = 0.145$), atrial fibrillation or flutter ($p = 0.236$), cerebrovascular events ($p = 0.450$), liver disease ($p = 0.115$), dyslipidemia ($p = 0.716$), cancer ($p = 0.811$), immunosuppression ($p = 0.854$), SAVR ($p = 0.792$), CAGB ($p = 0.109$), implanted cardiac devices ($p = 0.907$), chronic kidney disease ($p = 0.238$).

A multivariable binary logistic regression model (LR) was selected to identify possible factors associated with prolonged waiting, defined as waiting times above the 2021 – 2024 sample median. Firstly, univariable LRs were conducted with variables that could be expressed as covariates or as factors and the alternatives resulting in best model fit parameters were utilised in further modelling. In the first multivariable LR, all variables with a p-value below 0.1 in previous comparative analyses (Sections 6.6 and 6.7) were included. In the second iteration, additional variables described as significant in the literature were added. Variables with the highest Wald criterion p-values were removed sequentially, except those representing levels within the categorical variable (the year 2024 and the unspecified reasons group). A stepwise forward (by Likelihood ratio) selection method with virtually all predictors was used as an alternative approach, but it resulted in a worse-performing model than the theory-based approach. The final model showed a good fit, with the omnibus test of $p < 0.001$, Nagelkerke pseudoR^2 of 0.354, and Hosmer Lemeshow test of 9.527

(p = 0.30). Classification capability was satisfactory with specificity (percentage of correctly classified no-delay cases) of 77.2 %, sensitivity (percentage of correctly classified delayed cases) of 67.5 %, accuracy of 72.4 %, and Area under the curve test of 0.802 (Supplementary Materials Figure 12). The calibration plot presented a satisfactory matching of predicted and observed events across probability deciles, with minor deviations around mid-range probabilities (Supplementary Materials Figure 13). Outlier diagnostics were performed using Cook's distance, and no values equal to or above 1 were identified. No multicollinearity issues were detected, with all variance inflation factor values estimated at 1.019 or lower. Internal validation was performed using bootstrapping (1000 samples intended, 999 converged and were used for estimations) and showed good model stability for most predictors (Supplementary Materials Table 9). All confidence intervals remained stable except for the upper limit of the Other Reasons predictor. This could be explained by the small sample size of the predictor, only 7 cases (the second smallest reason group contained 68 observations), and the heterogeneous origin of the predictor. The bootstrapped significance of the Year 2021 was estimated at 0.037, indicating that it could be an important factor. Parameters of the final LR model were transferred to a generalised linear model with a log link to estimate the ratio of deviance and degrees of freedom (0.974), AIC (null model = 514.742; full model = 363.811), all confirming good model fit.

Key predictors were age, non-elective TAVI, year of intervention and reason groups. Increasing age was associated with shorter waiting times (OR 0.96; CI [0.929; 0.997]), as was non-elective TAVI (OR 0.09; CI [0.046; 0.189]). Cases performed in the year 2022 and 2023 had lower odds of reaching the delay threshold in comparison with the year 2024 (OR 0.31; CI [0.176; 0.55] and OR 0.35; CI [0.2; 0.621], respectively). Across reasons for delay, health-related and personal reason groups had a higher probability of having delayed waiting times (OR 3.6 [1.972; 6.555]; CI and OR 28.94; CI [10.815; 77.451] in reference to unspecified reason group (Table 6, Figure 10).

Table 6. Logistic regression summary for the prediction of TAVI waiting times

Parameter	B	S.E.	Wald	df	p-value	OR	95% CI for OR	
							Lower	Upper
Age	-0.038	.018	4.442	1	.035	0.962	.929	.997
Non-elective	-2.373	.360	43.365	1	<.001	0.093	.046	.189
Year 2021	-0.595	.305	3.811	1	.051	0.552	.304	1.002
Year 2022	-1.168	.291	16.098	1	<.001	0.311	.176	.550
Year 2023	-1.043	.289	13.025	1	<.001	0.352	.200	.621
Year 2024			19.357	3	<.001		*Reference*	
Reasons - Health	1.280	.306	17.441	1	<.001	3.595	1.972	6.555

Table 6. Logistic regression summary for the prediction of TAVI waiting times (continued)

Reasons - Personal	3.365	.502	44.899	1	<.001	28.942	10.815	77.451
Reasons - Other	1.717	.937	3.358	1	.067	5.570	.887	34.956
Reasons - NA			59.036	3	<.001		*Reference*	
Constant	3.624	1.471	6.070	1	.014	37.473		

B – unstandardized beta coefficient.
S.E. – standard error of the estimate for the regression model.
df – degrees of freedom.
OR – odds ratio, exponentiated beta coefficient.
CI – 95 % confidence interval for odds ratio estimate.

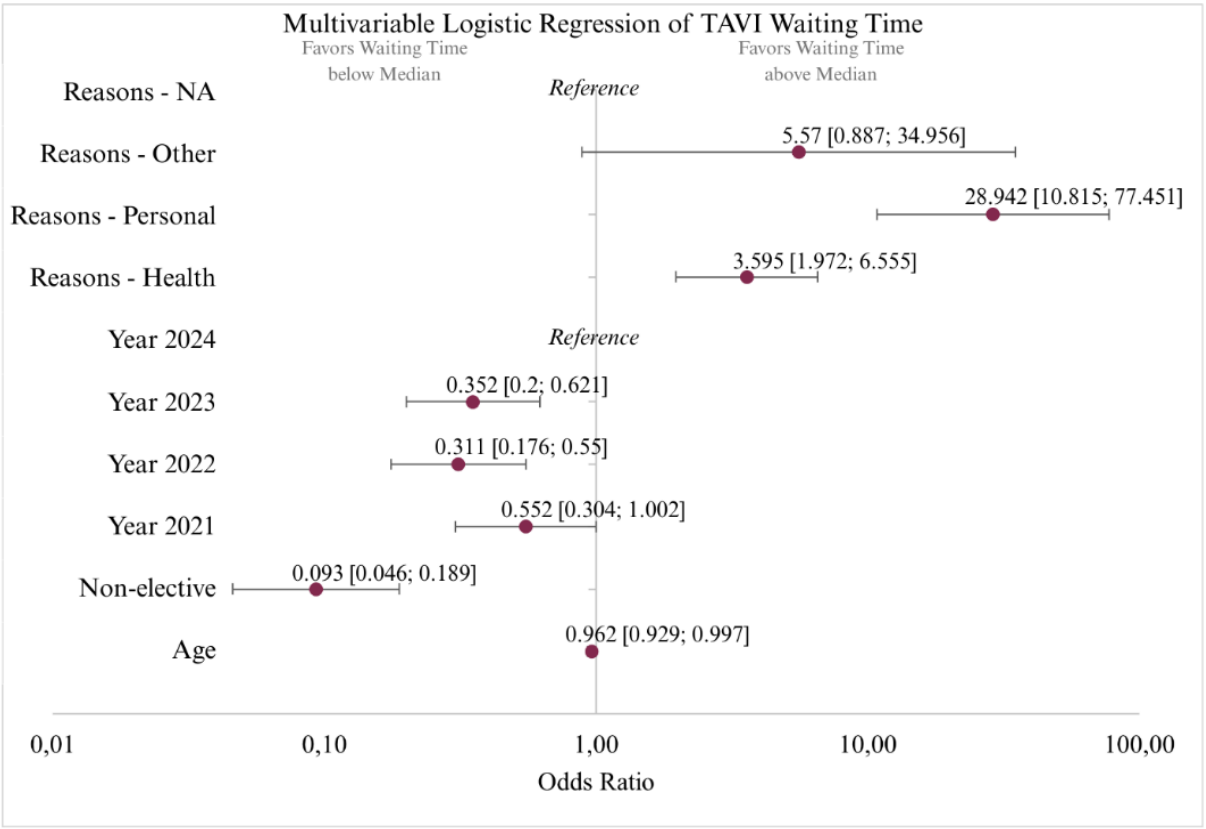


Figure 10. Forrest plot of Logistic regression results

7. DISCUSSION

7.1. Overview of the Results

TAVI volume has increased throughout 2009 – 2024, and the last four years were stably above 100 cases yearly. No significant sociodemographic differences were noticed (median age 80 years, comparably evenly distributed place of residence), except for sex – 64.89 % of the sample were female. Most of the patients belonged to the NYHA III class (67.79 %), had LVEF of 50 % or above (80.19 %), and were diagnosed with arterial hypertension (95.91 %) and dyslipidemia (80.65 %).

Overall, the total waiting time median in 2021 – 2024 was only slightly lower than the median of days throughout 2009 – 2024 (173 and 189.5 days, respectively); the mean waiting time was 338.3 days in 2009 – 2024 and 305.5 in 2021 – 2024. There were fluctuations year over year, the most recent being that waiting time in 2024 was virtually the same as in 2020, 2019, and 2017, longer than in 2018. Evaluation waiting time markedly decreased. However, procedural waiting time presented increasing tendencies, with PWT in 2024 being significantly longer than PWT in 2021, 2022 and 2023. Between-group comparisons showed a shorter total waiting time for the year 2022 compared to the year 2024, males, LVEF lower than 30 %, patients with a history of myocardial infarction, previous AoV surgery, and non-elective TAVI. TWT differences across clinical characteristics could suggest that more comorbid patients, possibly with worse clinical conditions at initial presentation, were triaged to receive TAVI sooner.

Most cases that waited longer than the 2021 – 2024 sample median did not have a specific cause for prolongation (57 %). The personal reason group had the highest total and evaluation waiting times median, but the shortest procedural waiting time of all delay groups. Females comprised more of the personal reasons group than the no-delay group. The no-delay group had significantly more patients with reduced ejection fraction than the unspecified delay group. Logistic regression indicated significant associations between the probability of prolonged waiting time and age, urgency, year of TAVI, and reason groups.

7.2. Comparison of Waiting Time Estimates with Other Regions

A study in the USA that defined waiting time from a recommendation for AVR showed 2.9 weeks (30) for both SAVR and TAVI in the period from 2008 to 2012. A Spanish study that counted waiting from TTE established a mean of 2.9 months (31) in 2014. A Swiss study analysed waiting time from diagnosis and presented a mean waiting time of 74.41 days (35) (2019 – 2021). A study in the UK provided a mean of 89.9 days (34) for a specialised local work-up centre (2020 – 2021), which is the total waiting time from diagnosis. Australian researchers estimated the waiting time from referral to hospital to be a median of 148 days (36) (2018 – 2021). In this context, the total TAVI waiting time in the study centre was the longest. One explanation could be that TAVI pathways across and within countries are highly variable, from Heart Team practices to standard workup workflow or the presence of a specialised heart valve outpatient clinic (29), all of which complicate the selection of representative data points for time calculations. It was not always clear how researchers defined waiting time date points; therefore, it would be helpful to include background information on the standard TAVI pathways of the researched region. In addition, many of the aforementioned countries were early adopters of the technology. By 2011, Germany had Europe's highest TAVI penetration rate, with 36.2 % of eligible TAVI candidates undergoing TAVI, followed by Switzerland with 35.5

% (58). Alternatively, in Poland, socioeconomically more similar to Lithuania, the penetration rate was estimated as 1.72 % (59) in 2011 and 18.65 % (60) in 2019, still not reaching the 2011 level of TAVI penetration in leading countries. Mylotte et al. (2013) (58) have identified a strong correlation between TAVI use and healthcare expenditure per capita; this indicator in Lithuania in 2021 was the lowest (1854.28 US dollars) among all the countries from where data on waiting times were published (61).

Procedural waiting time had a median of 78.5 and a mean of 117.92 days in 2009 – 2024, and a median of 89.5 and a mean of 116.97 days in 2021 – 2024. These times were longer than the majority of those discussed in the literature. One study analyzing socioeconomic effects estimated two workup waiting times that both were notably shorter: i) from CTA to TAVI as a median ranging from 14 – 20 days and ii) from coronary angiography to TAVI with a median range from 39 to 43 days (in the year 2012 – 2023) (27). This is a quite precise comparison opportunity in the current study design context, as the starting point for PWT here was either CTA or coronary angiogram and the long year span of the study itself. In Australian research, procedural waiting time was estimated as a median of 58 days in 2018 – 2021 (36). A Swiss study around the COVID-19 pandemic period (2019 – 2021) provided a mean of 47.77 days from referral (as an intermediate data point following diagnosis date) to TAVI (35). Another study in Canada established a median of 34 days waiting from acceptance in MDT to TAVI (2010 – 2016) (19). In the UK-based study comparing waiting times by the type of the centre that made the referral (2020 – 2021), the mean waiting time from MDT discussion to AVR for the local centre (without surgical or TAVI services) was 32 days, and for traditional pathway, it was 126 days (34). Thus, VUH SK had slightly shorter procedural waiting times than standard UK centres but markedly longer than local workup centres.

The evaluation waiting time in this study was estimated as a median of 62.5 days and a mean of 220.36 days in 2009 – 2024, a median of 49 days and a mean of 188.48 days in 2021 – 2024. In a Canadian study, the time from referral to acceptance at MDT was estimated to be a median of 54 days (2010 – 2016) (19). Swiss TAVI study showed a mean of 26.64 days from diagnosis to the referral waiting time (2019 – 2021) (35). Work-up time (referral to approval by MDT) was estimated at a median of 78 days in an Australian study between 2018 and 2021 (36). In this context, VUH SK evaluation waiting time seems more consistent with the situation in other countries than TWT and PWT. However, a three-and-a-half-fold larger mean compared to the median and a larger interquartile range than that of PWT imply high variability of evaluation duration among the sample. It might indicate issues with the specificity of the definition of the first data point – some of the cases might have fallen out of the follow-up for part of the waiting time included in the study; especially, this could have been the case in the personal reasons for delay group. Therefore, some of the estimated

evaluation time might not have been waited. In any case, from the comparisons with other studies and tendencies of the last 4 years, it seems that PWT, which had more robust definitions, is becoming more accountable for prolonged TWT.

7.3. Predictors of Waiting Times in 2021 – 2024

Between-group comparisons revealed significant differences in TWT across different LVEF group patients, with the severely reduced LVEF group receiving TAVI faster than the preserved LVEF and moderately reduced LVEF groups. This association corresponds to other studies where heart failure was found to shorten TAVI waiting time: previous heart failure (HF) had a hazard ratio (HR) of 1.18 (hazard being shorter waiting time) (19), and in another study, congestive HF had a 1.29 HR (20).

Patients with a history of myocardial infarction had shorter waiting times (145 versus 182 median days). Other studies did not specifically report differences between waiting times across myocardial infarction status, except one study found that ischaemic heart disease predisposes shorter waiting times with HR of 1.12 (20), one study analysing angina at rest that found a strong protective effect against waiting longer than 2 months with an odds ratio of 0.3 (31). In the current study, patients with previous aortic valve surgeries had shorter waiting times (92 versus 174 days). This is in accordance with a study by Henning et al. (2020)(20) that demonstrated a previous AoV surgery association with shorter waiting times at a HR of 1.47; analysis also indicated significant PCI and CAGB HRs of 1.13 and 1.2, respectively. However, our between-group comparisons of waiting times across PCI or CAGB statuses were insignificant, they remained so in logistic regression modelling. TAVI urgency is an obvious category for significant differences in waiting times; nevertheless, the non-elective group had variable waiting durations, with Q1 being 14.75 and Q3 being 85 days, likely due to some of the initially elective patients deteriorating and requiring non-elective TAVI. Though not significantly, the proportion of non-elective TAVIs increased from 17.9 % in 2021 to 20 % in 2024, which could have indirectly contributed to elective patients potentially waiting longer.

Documented reasons for prolonged waiting time were exploratorily gathered, and adjustment by a median of TWT showed that the most commonly documented reasons were personal (23.88 %). Other studies did not perform such analyses; however, in the case of this study, there were no reliable criteria to separate falling out of the follow-up and inclusion back into the waiting list following patient refusal. Therefore, it was important to try to capture those cases that might have had prolonged waiting times due to reasons at least directly independent of health status and healthcare. In one way, this enables the estimation of a median waiting time that is more similar to those in the registries in a practical sense. It also allows the investigation of different reason groups. Total waiting time and evaluation waiting time were the longest in the Personal and Other reason groups; however,

the longest procedural time was observed in the health-related reasons group. Such an increase might be due to additional work-up following standard TAVI evaluation. The proportion of patients with previous PCI was significantly larger in the health-related group compared to other groups, as between group (PCI or no PCI) comparisons showed no significant difference, and PCI's included could have been done long before the onset of AS as well as after the TAVI work-up, this significant difference could be a reflection of higher comorbidity burden of the health-related delay group. In the literature, a greater comorbidity burden was associated with prolonged waiting time (32).

Logistic regression showed age (OR 0.96), the year 2022 (OR 0.31) and 2023 (OR 0.35) (in relation to the year 2024), and non-elective TAVI (OR 0.093) to be associated with shorter waiting times and personal and health reasons to be associated with longer waiting times. Other studies identified age as mainly associated with shorter waiting times. Both Elbaz-Greener et al. (2018) (19) and Albassam et al. (2020) (32) established an HR of 1.01 for the hazard of having shorter waiting times. Gonzalez Saldivar et al. (2019) (31) found an OR of 0.96 for waiting longer than 2 months. However, Stehli et al. (2023) (36) identified a correlation between age and longer procedural waiting time in women, but age and longer work-up waiting time correlated in men. Wijeysundera et al. (2020) (33) also found age associated with longer waiting times. Non-elective TAVI as a protector against prolonged waiting is not a novel insight; nevertheless, this indicated that the model complied with real-world patterns. The significance of the year when intervention was performed was previously described by Albassam et al. (2020) (32), with earlier years (2012 – 2016) having an HR of 1.08 – 1.78 for shorter waiting time, thus suggesting, despite technological progress and patient care optimisation, waiting times tend to lengthen.

A Canadian study (19) in 2018 determined strong tendencies of decreasing waiting time in the pre-funding period (from 322 to 118 days) and a significant reduction in waiting time after the funding era, followed by further stabilization of waiting time at a median of 82 – 84 days, though the changes in funding sums were not presented. In the current case, no clear trend was visible before and after governmental funding establishment; dedicated funds fluctuated and even though larger financial injections started at the end of 2019, the shortest waiting times were in 2022 and 2023. It might be that the results of 2020 and 2021 were significantly affected by the COVID-19 pandemic; however, it would not explain the increase in total and procedural median waiting times in 2024. One explanation for the total waiting time increase for patients in 2024 could be a higher prevalence of comorbidities (chronic kidney disease, dyslipidemia, NYHA III class, peripheral arterial disease) compared to some of the previous years. Given the reduction in evaluation waiting time, combined with the considerably higher volume of CTA referrals (in relation to TAVI volume) and the limited annual transcatheter valves' availability due to budget constraints, longer PWT – and consequently

prolonged TWT – might indicate insufficient supply or other patient-independent factors contributing to a potential bottleneck effect on the waitlist.

The majority of the VUH SK patients were female. This stands out in the context of other studies in waiting time, where women consisted the lesser proportion from 40.5 % (34) to 49.8 % (28) of the samples; landmark TAVI trials had female representation from 31 to 54 % (62) and in registries, the proportion ranges from 44 to 56 % (62). A couple of explanations for this disparity might be possible. For one, women have a longer life expectancy than men, and this discrepancy is particularly expressed in Lithuania, where men have the fourth lowest life expectancy, paired with the second largest women-to-men ratio (113.9) in the EU (63). It could be hypothesised that this tendency might be apparent in sociodemographically similar Baltic and Eastern European regions. Females had significantly longer waiting times than men (187 and 153 days, respectively), and this was in concordance with other studies: a Canadian study found 0.87 HR (HR<1 indicating longer waiting times) of being a female (32), in Australian study total waiting time was median 156 days for females and median 140 days for males and during the pandemic, this difference escalated to 168 and 135 days, respectively (36). The current study showed that significantly more females delayed TAVI for personal reasons. Stehli et al. (2023) (36) hypothesised that women may receive TAVI later due to more fibrous and less calcific changes of the AoV. Additionally, the findings of this study could suggest that this difference may be, to some extent, socially or psychologically rooted. Previously conducted studies on treatment-related decision-making in breast cancer patients emphasised the relevance of personal beliefs, experience, characteristics (64), individual, family, medical care and community domains (65).

7.4. Limitations

One of the main study limitations lies in the retrospective nature of the study's design. Many studies in the field were based on registry data, providing more exact estimations. This impedes the possibility of intercomparisons with other studies or a comprehensive exploration of only health status or healthcare-dependent waiting time. However, the current research also suggests an outlook on genuine today's patient pathway in the tertiary centre – some patients hesitate to undergo timely intervention.

There might be other confounding variables that were not identified. This study did not analyse frailty, which was often referenced in TAVI waiting time publications. It could be sensible to supplement the current analysis with procedural characteristics like access site and estimates reflecting comorbidity burden, such as the Charlson Comorbidity Index (66), EuroSCORE II, the Society of Thoracic Surgeons risk models (67). EuroSCORE II evaluations in this study were not analysed in greater depth because they were partly extracted from medical records and partly

estimated retrospectively, which could not be as exact as prospective estimation; therefore, the estimates of EuroSCORE II were considered with reservation.

8. SUMMARY AND RECOMMENDATIONS

This study was the first to analyse TAVI waiting times in a northeastern Baltic region country. The results suggest the following:

1. The TAVI patient population predominantly consisted of individuals aged 75 years or older, more females and was geographically evenly distributed. Cardiovascular and renal comorbidities were the most prevalent.
2. Total waiting time fluctuated throughout 2009 – 2024, and the median estimation of total waiting time in 2021 – 2024 was longer than most findings in the literature. A trend of decreasing evaluation waiting time and increasing procedural waiting time is evident, with the latter accounting for the larger part of total waiting time since 2021.
3. Patients who were female, belonged to the preserved ejection fraction group, and had no history of myocardial infarction or aortic valve surgery waited significantly longer for TAVI. Older age, intervention in earlier years, and non-elective TAVI could be potential predictors of total waiting time below the 2021 – 2024 median (173 days). A substantial number of TAVI-received patients had prolonged waiting times due to personal and health-related reasons.

Current total waiting times are associated with waitlist risks of increased mortality and morbidity and indicate a need for efforts to reduce the waiting duration. While the findings of this study cannot indicate causality, based on observed patterns, it might be reasonable to propose a reevaluation of TAVI funding or explore additional sources of funds in order not only to keep up with the increasing demand but also to reduce waiting times to a relatively safe interval. Meanwhile, effective patient risk stratification is essential to identify those needing a timely intervention, as is attention to streamlining additional post-standard-TAVI evaluation for patients in the health-related delay group. For future research, it might be valuable to explore what factors determine patient refusal or indecision and provide insights on addressing this aspect in a clinical setting. In addition, the development of variables evaluating hospital-dependent TAVI processes and how they affect waiting times might be beneficial. It could be justified to reexplore previously identified outcomes of prolonged waiting times in regions beyond Western high-income countries, as the predictors of waiting times and level of TAVI adoption differ; thus, different patterns might emerge that could lead to more context-specific TAVI waiting time benchmarks.

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10. SUPPLEMENTARY MATERIALS

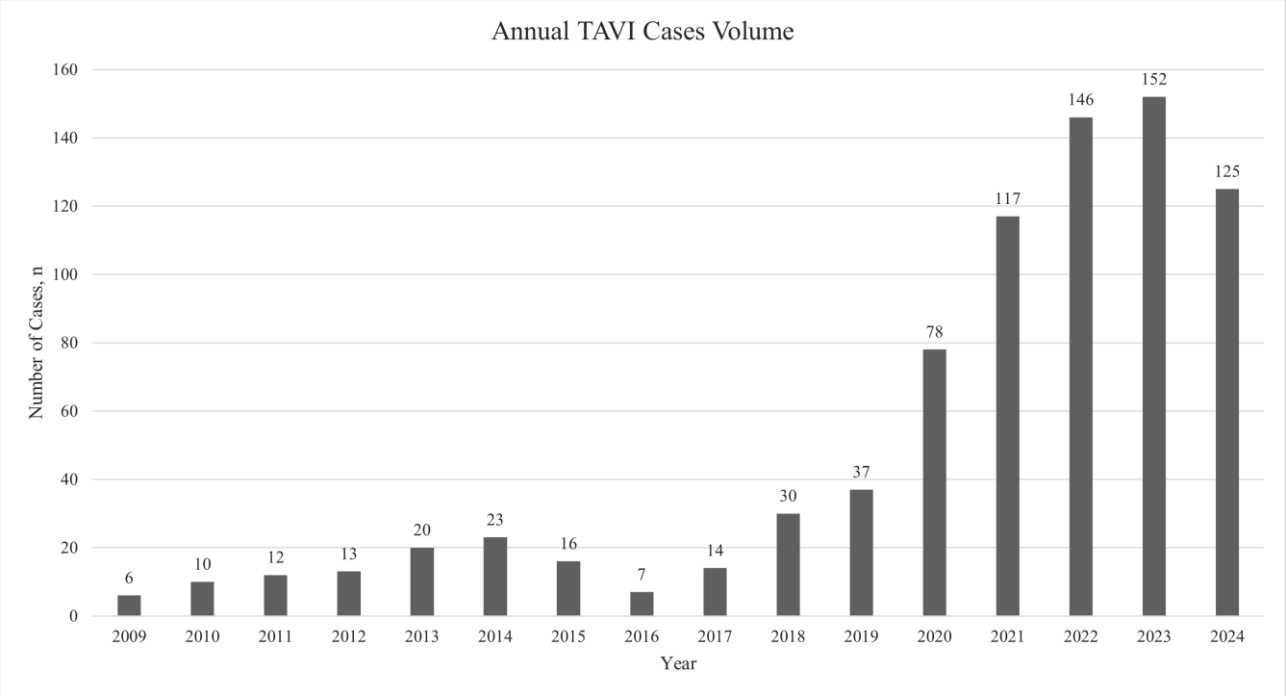

Figure 11. The number of annual TAVI cases included in this study after the exclusion criteria were applied

Table 7. Prevalence of sociodemographic and health characteristics during 2021 - 2024

Variables	2021	2022	2023	2024	p-value	Effect size[1]	CI
Age	80 (76; 83)	79 (76; 82)	80 (76; 84)	80 (77; 83)	0.472	0.001	-0.005; 0.02
Arterial hypertension	114 (97.4)	143 (97.9)	149 (98)	123 (98.4)	0.690	0.02	0.02; 0.14
Atrial fibrillation	42 (35.9)	56 (38.4)	56 (36.8)	55 (44)	0.553	0.06	0.03; 0.17
BMI	29.67 (24.94; 33.89)	30.07 (27.18; 31.91)	28.39 (25.51; 32.21)	28.62 (24.73; 32.6)	0.145	0.005	-0.003; 0.03
Cancer	11 (9.5)	14 (9.6)	18 (11.8)	6 (4.8)	0.236	0.09	0.04; 0.18
Cerebrovascular events	15 (12.8)	16 (11)	16 (10.5)	16 (12.8)	0.903	0.03	0.02; 0.15
Chronic kidney disease	48[a,b] (41)	**47[b] (32.2)**	65[a,b] (42.8)	**62[a] (49.6)**	**0.034**	**0.13**	**0.07; 0.22**

Table 7. Prevalence of sociodemographic and health characteristics during 2021 – 2024 (continued)

COPD	8 (6.8)	13 (8.9)	15 (9.9)	14 (11.2)	0.690	0.05	0.03; 0.15
Diabetes	29 (24.8)	40 (27.4)	43 (28.3)	28 (22.6)	0.704	0.05	0.03; 0.16
Dyslipidemia	99[a] (84.6)	123[a] (84.2)	141[a,b] (92.8)	120[b] (96)	**0.002**	**0.16**	**0.1; 0.25**
Liver diseases	2 (1.7)	4 (2.7)	1 (0.7)	2 (1.6)	0.578	0.06	0.03; 0.16
LVEF <50 %	28 (23.9)	28 (19.2)	26 (17.1)	25 (20)	0.486	0.06	0.03; 0.16
NYHA I Class	0[a] (0)	5 [a] (3.4)	5 [a] (3.3)	1 [a] (0.8)	**0.002**	**0.12**	**0.10; 0.18**
NYHA II Class	26 [a, b] (22.8)	41 [a, b] (28.3)	**55 [b] (36.7)**	**23 [a] (18.4)**			
NYHA III Class	81 [a, b] (71.1)	96 [a, b] (66.2)	**88[b] (58.7)**	**97 [a] (77.6)**			
NYHA IV Class	7 [a] (6.1)	3 [a] (2.1)	2 [a] (1.3)	4 [a] (3.2)			
PAPS	41 (35; 51)	39.5 (34.75; 53.25)	37 (30; 50)	43 (35; 55.75)	0.113	0.006	-0.003; 0.04
Periferial Arterial Disease	21[a, b] (17.9)	29[a, b] (19.9)	**14[b] (9.2)**	**18[a] (22.4)**	**0.018**	**0.14**	**0.08; 0.22**
Previous AoV Surgery	5 (4.3)	1 (0.7)	4 (2.6)	7 (5.6)	0.086	0.11	0.05; 0.2
Previous MI	19 (16.2)	26 (17.8)	25 (16.4)	29 (23.2)	0.439	0.07	0.03; 0.17
Urgency (non-elective)	21 (17.9)	24 (16.4)	28 (18.4)	25 (20)	0.8995	0.03	0.02; 0.14
Sex (female)	79 (67.5)	92 (63)	94 (61.8)	80 (64)	0.803	0.04	0.02; 0.15
Vilnius inhabitants	59 (50.4)	78 (53.4)	77 (50.7)	64 (51.2)	0.957	0.02	0.02; 0.14

For quantitative variables medians, Q1 and Q3 are provided in cells, and the effect size was calculated using the eta squared H method. For categorical variables, count values and percentage of the total column (reason group) are provided in the cells, and the effect size was calculated using Cramer's V.

* Pairs of variables marked with the same number of asterisks (*) indicate statistically significant Kruskal-Wallis post-hoc pairwise comparisons ($p < 0.05$).

[a, b] Statistically significantly different groups according to the Chi-square post hoc Z-test were indicated by letters in cell values.

Table 8. Total waiting time differences between groups (in days)

Variable		Median	Q1	Q3	IQR	n	p-value	Effect size	CI
Age	< 75 year old	178.5	86.5	283	196.5	86	0.546	0.48	0.414; 0.546
	75 or older	172	98.0	314.75	216.75	454			
Arterial hypertension	No	85	72	140.5	68.5	11	0.123	0.364	0.223; 0.533
	Yes	174	98	310	212	529			
Atrial fibrillation	No	183	98.5	319	220.5	331	0.148	0.537	0.487; 0.586
	Yes	156	91	295	204	209			
Cancer	No	172	94	304.5	210.5	490	0.752	0.514	0.429; 0.597
	Yes	174	85	355	270.0	49			
Cerebrovascular events	No	173	93	310	217	477	0.838	0.492	0.417; 0.567
	Yes	176	98.5	296.5	198	63			
Chronic kidney disease	No	180	99.25	314.75	215.50	318	0.073	0.545	0.496; 0.594
	Yes	160	78.25	293	214.75	222			
COPD	No	172	92.25	304.5	212.25	490	0.830	0.491	0.408; 0.575
	Yes	183	100.25	343.5	243.25	50			
Diabetes	No	174	96.5	323.50	227	399	0.412	0.523	0.468; 0.578
	Yes	162.5	89	273.25	184.25	140			
Liver disease	No	170	93	308.5	215.5	531	0.311	0.402	0.239; 0.59
	Yes	219	211	315	104	9			
Dyslipidemia	No	156	72	348	276	57	0.447	0.469	0.392; 0.548
	Yes	174	97.5	308.5	211	483			
LVEF	<30*, **	58	15	141	126	21	**<0.001**	**0.036**	**0.01; 0.08**
	30-40*	143	50.5	408	357.5	54			
	41-49	141	68	237	169	31			
	>=50**	182	113	314	201	433			
NYHA	I class	168	89	438.5	349.5	11	0.0538	0.009	-0.003; 0.04
	II class	203	120	355	235	145			
	III class	169	92	298.25	206.25	362			
	IV class	88	33.25	227	193.75	16			
Peripheral arterial disease	No	170	98	303	205	448	0.858	0.494	0.43; 0.559
	Yes	189	89.5	331.5	242	92			
	No	174	98	314.00	216.00	523	**0.028**	0.656	

Table 8. Total waiting time differences between groups (in days) (continued)

Previous AoV Surgery	Yes	92	35	211.00	176.00	17			0.522; 0.769
Previous MI	No	182	105	324	219	441	**0.005**	**0.59**	**0.528; 0.649**
	Yes	145	67	251.5	184.5	99			
Urgency	Elective	196.5	130.25	330	200	442	**<0.001**	**0.815**	**0.774; 0.85**
	Non-elective	36	14.75	85	70	98			
Sex	Female	187	106	315	209	345	**0.015**	**0.563**	**0.513; 0.612**
	Male	153	84	286.5	202.5	195			
Vilnius inhabitants	No	168.5	87.25	292.25	205	262	0.403	0.479	0.431; 0.528
	Yes	176	99	335.25	236.25	278			

* Pairs of variables marked with the same number of asterisks (*) indicate statistically significant pairwise comparisons ($p < 0.05$).
The effect size for comparisons between 2 categories (Mann-Whitney U test) was calculated using Common language effect size, between 3 or more categories (Kruskal-Wallis test) – eta squared H.

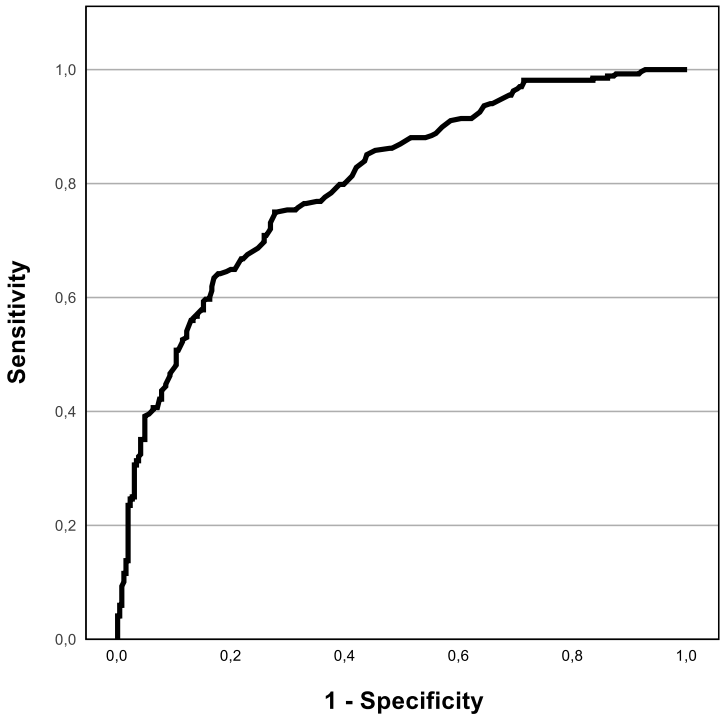

Figure 12. The area under the curve of predicted probabilities by the logistic regression model

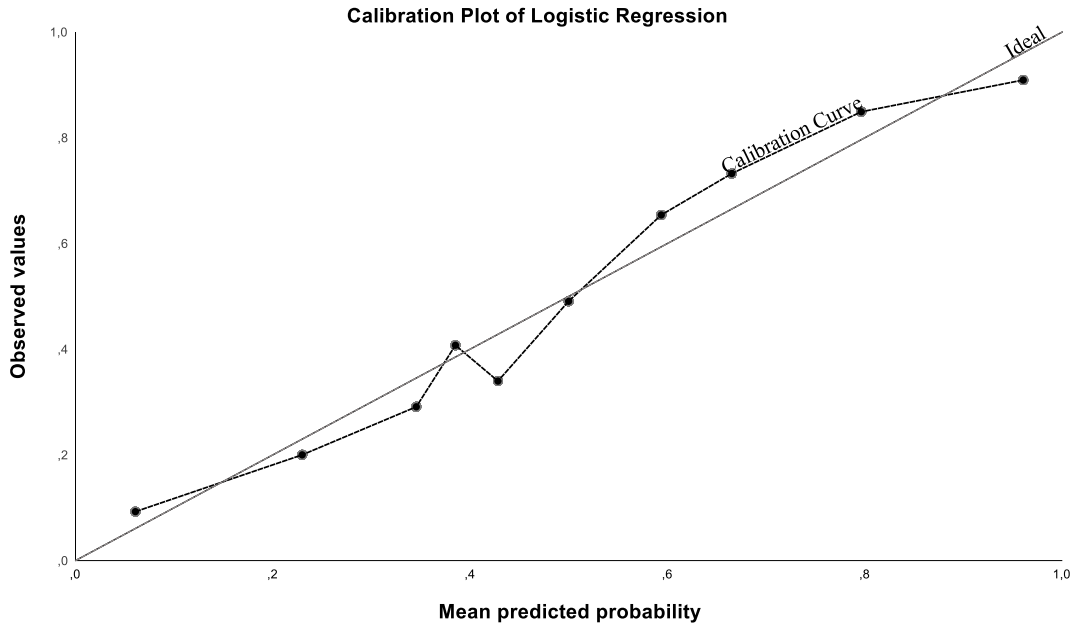

Figure 13. Calibration Plot of Logistic Regression Model

Table 9. Results of Logistic Regression Model Bootstrapping

Parameter	B	Bias	S.E.	p-value	OR	CI of OR	
						Lower	Upper
Age	-0.038	-.001[b]	.018[b]	.023[b]	0.962	0.929	0.995
NonElective	-2.373	-.111[b]	.388[b]	.001[b]	0.093	0.037	0.165
Year 2021	-0.595	-.006[b]	.296[b]	.037[b]	0.552	0.313	0.997
Year 2022	-1.168	-.028[b]	.283[b]	.001[b]	0.311	0.173	0.526
Year 2023	-1.043	-.025[b]	.298[b]	.001[b]	0.352	0.188	0.598
Reasons - Health	1.280	.057[b]	.290[b]	.001[b]	3.595	2.181	6.699
Reasons - Personal	3.365	.201[b]	1.110[b]	.001[b]	28.942	10.444	173.643
Reasons - Other	1.717	2.748[b]	7.333[b]	.067[b]	5.570	0.650	11736858194
Constant	3.624	.097[b]	1.438[b]	.009[b]	37.473	2.881	775.106

B – unstandardized beta coefficient.
S.E. – standard error of the estimate for the regression model.
OR – odds ratio, exponentiated beta coefficient.
CI – 95 % confidence interval for odds ratio estimate.
[b] Based on 999 samples.