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The Relationship Between Medication Burden and 30-day Mortality in Patients Undergoing Transcatheter Aortic Valve Implantation

Transkateter Aort Kapak İmplantasyonu Uygulanan Hastalarda İlaç Yükü ile 30 Günlük Mortalite Arasındaki İlişki

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ABSTRACT

Background: Transcatheter aortic valve implantation (TAVI) is a treatment method that is particularly relevant to the geriatric population and is applicable to fragile patients. However, data on the predictive value of medication burden, which is a component of fragility, for post-TAVI clinical outcomes are very limited. The aim of this study was to evaluate the effect of polypharmacy on 30-day clinical outcomes, especially mortality, in patients undergoing TAVI.

Materials and Methods: In this retrospectively designed study, 225 patients who underwent TAVI between December 2017 and December 2021 were examined. The patients' medications were divided into three groups according to the Multum Lexicon Drug Database: heart failure drugs, cardiovascular drugs, and non-cardiovascular drugs. Hyperpolypharmacy (HPP) was defined as the use of ten or more medications. Clinical outcomes were compared between the groups with and without HPP.

Results: According to the analysis, HPP was present in 39.1% of patients. The HPP group had a significantly higher 30-day mortality rate than the non-HPP group. Additionally, major bleeding was more common in the HPP group. Multivariate logistic regression analysis revealed that HPP was independently associated with 30-day mortality.

Conclusion: Our study highlights the high prevalence of medication burden in patients undergoing TAVI and the association between HPP and adverse clinical outcomes. HPP should be considered as a potential risk factor for 30-day mortality and major bleeding in patients with TAVI. Strategies such as avoiding unnecessary drug use and reducing the number of medications should be implemented in the geriatric assessment of patients with TAVI to optimize outcomes. Further studies are needed to confirm these findings and explore potential interventions to improve medication management in patients with TAVI.

Keywords: Hyperpolypharmacy, aortic stenosis, transcatheter aortic valve implantation, 30-day mortality, aging

ÖZ

Amaç: Transkateter aort kapak implantasyonu (TAVI), özellikle geriatrik popülasyonu ilgilendiren ve frajil hastalara uygulanan bir tedavi yöntemidir. Ancak TAVI sonrası klinik sonuçlar için frajilitenin bir komponenti olan ilaç yükünün prediktif değerine dair veriler çok sınırlıdır. Bu çalışmanın amacı, TAVI uygulanan hastalarda 30 günlük mortalite ve majör kanamayı öngörmede hiperpolifarmasinin (HPP) prognostik değerini araştırmaktır.

Gereç ve Yöntemler: Retrospektif olarak tasarlanan bu çalışmaya Aralık 2017 ile Aralık 2021 arasında TAVI uygulanan toplam 225 hasta dahil edildi. Hastaların kullanmış olduğu ilaçlar Multum Lexicon İlaç Veri Tabanı'na göre üç gruba ayrıldı: kalp yetmezliği (KY) ilaçları, KY olmayan kardiyovasküler ilaçlar ve kardiyovasküler olmayan ilaçlar. HPP, on veya daha fazla ilaç kullanımı olarak tanımlandı. HPP ve klinik sonuçlar arasındaki ilişki, çok değişkenli lojistik regresyon modelleri kullanılarak analiz edildi.

Bulgular: Ortalama toplam ilaç sayısı 9'du ve hastaların %39,1'inde HPP mevcuttu. HPP grubu, non-HPP grubuyla karşılaştırıldığında önemli ölçüde daha yüksek 30 günlük ölüm oranına sahipti. Ayrıca, HPP grubunda majör kanama daha sık olarak saptandı. Çok değişkenli lojistik regresyon analizi, HPP 30 günlük mortalite ile bağımsız olarak ilişkili olduğunu ortaya koydu.

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ÖZ

Sonuç: Çalışmamız, TAVI uygulanan hastalarda ilaç yükünün yüksek prevalansını ve HPP ile olumsuz klinik sonuçlar arasındaki ilişkiyi vurgulamaktadır. HPP, TAVI hastalarında 30 günlük mortalite ve majör kanama için potansiyel bir risk faktörü olarak düşünülmelidir. Sonuçları optimize etmek için TAVI hastalarının geriatrik değerlendirmesinde gereksiz ilaç kullanımından kaçınmak ve ilaç sayısını azaltmak gibi stratejiler uygulanmalıdır. Bu bulguları doğrulamak ve TAVI hastalarında ilaç yönetimini iyileştirmeye yönelik potansiyel müdahaleleri araştırmak için daha ileri çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Hiperpolifarmasi, aort stenozu, transkateter aort kapak implantasyonu, 30-günlük mortalite, yaşlanma

Introduction

Aortic stenosis (AS) is a prevalent disease among the elderly population. The global demographic shift toward an aging population has increased the number of elderly patients requiring invasive cardiological treatments or cardiac surgery. From 1992 to 2008, there was an increase in the percentage of elderly patients receiving heart surgery in Germany, with the proportion rising from 2.3% to 10.8% (1). In recent years, this trend has continued to accelerate, with the need for surgical or interventional treatment primarily driven by severe AS. Although aortic valve surgery is considered the standard of care, transcatheter aortic valve implantation (TAVI) has become a common treatment method for patients with underlying conditions and risk factors. TAVI is a minimally invasive, safe, and effective procedure that presents a valuable therapeutic option for patients with severe AS and a high risk of complications during traditional surgery (2). However, despite its many benefits, adverse events after the procedure cannot be underestimated (3).

Various parameters have been studied for their association with poor clinical outcomes in patients undergoing TAVI, with comorbid burden and frailty emerging as noteworthy issues (4,5). Elderly and high-risk patients often have multiple comorbidities that impact their prognosis after the procedure. Furthermore, the use of multiple drugs is a significant risk factor associated with the course of multiple diseases. Polypharmacy, defined as the use of five or more drugs, has been categorized as a geriatric syndrome and is frequently observed in elderly patients (6). Approximately 40% of individuals over 65 use five or more drugs. In addition to comorbidities, polypharmacy leads to negative outcomes due to drug-drug interactions and increased drug side effects (7). Prior research indicates that polypharmacy is associated with several adverse events, including declines in functional capacity, increased drug interactions, length of hospital stay, recurrent hospital admissions, and mortality (8). The use of drugs in cardiovascular diseases is particularly high, with hyperpolypharmacy (HPP) defined as the use of ten or more drugs. HPP is detected in one out of every four patients with heart failure (HF) and predicts poor outcomes (9). Furthermore, HPP predicts worse outcomes, exacerbating frailty in elderly patients.

Despite numerous studies on the effects of polypharmacy on clinical outcomes in geriatric patients, there is a significant gap in the literature regarding the association between polypharmacy and clinical outcomes in patients who have undergone TAVI. The focus of this research is to assess how HPP affects 30-day mortality and Valve Academic Research Consortium-3 (VARC-3) endpoints among patients who have undergone TAVI.

Materials and Methods

Study Population

In this retrospective study, the records of 257 consecutive patients with symptomatic severe AS who underwent TAVI in a tertiary center between December 2017 and December 2021 were reviewed. The heart team, comprising cardiovascular surgeons, cardiologists, anesthesiologists, and pulmonologists, decided on TAVI after assessing preoperative risk using the Society of Thoracic Surgeons (STS) risk calculator system. Severe AS was defined according to the European Society of Cardiology valvular heart disease guidelines (10). Exclusion criteria were absence of medical records. Demographic, clinical, biochemical, and echocardiographic evaluations were recorded for all patients. The study protocol was approved by the University of Health Sciences Türkiye, Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital Ethics Committee in April 2021 (decision no: 2021/38, date: 27.04.2021), and the study was conducted in accordance with the principles outlined in the Declaration of Helsinki.

Definition of Hyperpolypharmacy

In this study, we used the classification of medications according to the Multum Lexicon Drug Database, as used by Unlu et al. (11) on patients with HF. The categorization comprises three primary clusters of medicines: HF medications, cardiovascular system drugs other than HF, and drugs used to treat non-cardiovascular diseases (12).

At admission, patients were questioned regarding their drug usage, and their drug containers were checked and recorded in their medical records. These records were scanned retrospectively, and the number and types of drugs used by the patients were determined. While studies generally accept the presence of polypharmacy (≥5 drugs) as a predictor, the high rate of polypharmacy in the TAVI patient group encouraged us to evaluate HPP (≥10 drugs).

Endpoints

The focus of this study was to assess the impact of HPP on 30-day mortality rates. To complement this primary endpoint, several secondary endpoints were also investigated, including major bleeding, stroke, myocardial infarction, acute kidney injury (AKI), major vascular complications, and the need for a new permanent pacemaker (PACE), as outlined by the VARC-3 (13). The definition of major bleeding is outlined by the VARC-3 consortium as type 2 (major), type 3 (life-threatening), and type 4 (leading to death) bleeding. Accordingly, the spectrum ranging from the need for at least 2-4 units of whole blood/red blood cells transfusion to life-threatening or fatal bleeding has been considered to be within the scope of major bleeding (13).

Statistical Analysis

The Statistical Package for the Social Sciences, version 24.0 (SPSS Inc., Chicago, Illinois, USA), was used to analyze the data. The normal distribution of variables was assessed through visual methods such as histograms and probability curves, and analytical methods including the Kolmogorov-Smirnov and Shapiro-Wilk tests. Numerical variables showing normal distribution were presented as mean ± standard deviation, whereas those not showing normal distribution were expressed as median (interquartile range) and categorical variables as percentage (%). For statistical analysis of numerical variables between groups, either Student's t-test or Mann-Whitney U test was used, whereas chi-square or Fisher's Exact test was employed for categorical variables. To identify the independent predictors of 30-day mortality, univariate logistic regression analysis was performed first, and subsequently, multivariate logistic regression analysis was conducted using the parameters that were significant (p-value <0.1) in the initial analysis. A p-value of <0.05 was considered significant throughout the study.

Results

Upon screening for inclusion and exclusion criteria, we enrolled 225 patients who underwent TAVI. The patient population had a mean age of 78.4 years, with females accounting for 62.2% of the cohort. Based on HPP status, patients were stratified into two groups, with 88 patients in the HPP group and a HPP rate of 39.1%. Table 1 outlines the demographic and clinical characteristics of the study population. In the HPP group, hyperlipidemia [50 (36.2) vs. 59 (67.0), p<0.001] and atrial fibrillation [22 (16.1) vs. 30 (34.1), p=0.002] were observed more frequently, and the aortic valve area (AVA) was lower in the HPP group (0.77±0.14 vs. 0.72±0.13, p=0.024). No significant difference was detected between the groups for other clinical and demographic characteristics, except for a higher STS score in the non-HPP group.

Table 2 presents the medication profile according to the HPP status. The mean medication count was 9 for the entire cohort, with HPP and non-HPP groups having 12 and 7 mean medication counts, respectively. Beta-blockers were the most commonly used drug group, with all drug groups, except antiplatelet agents and bronchodilators, being used at a higher rate in the HPP group.

Table 3 outlines the clinical endpoints of the patients based on HPP status. HPP was associated with higher 30-day mortality [2 (1.5) vs. 8 (8.9), p=0.016] and major bleeding [11 (8.1) vs. 21 (23.3), p<0.001]. Although stroke, AKI, myocardial infarction, and the need for a new permanent PACE were proportionally higher in the HPP group, no statistically significant difference was detected between the two groups. Major vascular complications were also higher in the HPP group. A comparison of 30-day mortality and VARC-3 outcomes based on HPP status is shown in Figure 1.

To identify independent predictors of 30-day mortality in patients undergoing TAVI, we performed univariate logistic regression analysis (Table 4). The analysis revealed

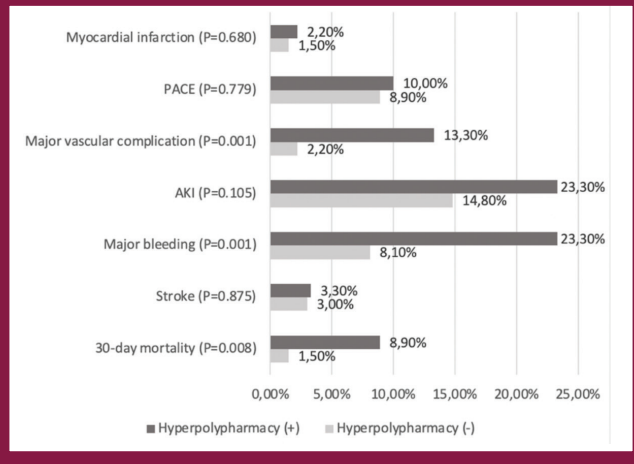

Figure 1. Comparison of 30-day mortality and VARC-3 outcomes in the presence of hyperpolypharmacy

PACE: Pacemaker, AKI: Acute kidney injury, VARC-3: Valve Academic Research Consortium-3

Table 1. Baseline clinical and echocardiographic characteristics according to the presence of hyperpolypharmacy

Variables	Total (n=225)	Hyperpolypharmacy (-) (n=137)	Hyperpolypharmacy (+) (n=88)	p-value
Age, years	78.4±7.9	78.2±8.1	78.7±7.7	0.614
Gender (male), n (%)	85 (37.8)	55 (40.1)	30 (34.1)	0.361
Hypertension, n (%)	155 (68.9)	91 (66.4)	64 (72.7)	0.319
Previous cardiac surgery, n (%)	51 (22.7)	27 (19.7)	24 (27.3)	0.186
Coronary artery disease, n (%)	137 (60.9)	82 (59.9)	55 (62.5)	0.691
COPD, n (%)	133 (59.1)	82 (59.1)	51 (58)	0.777
Diabetes mellitus, n (%)	92 (40.9)	53 (38.7)	39 (44.3)	0.402
Hyperlipidemia, n (%)	109 (48.4)	50 (36.5)	59 (67)	<0.001
CKD, n (%)	72 (32)	44 (32.1)	28 (31.8)	0.963
PAD, n (%)	73 (32.4)	47 (34.3)	26 (29.5)	0.457
CVD, n (%)	8 (3.6)	4 (2.9)	4 (4.5)	0.520
Atrial fibrillation, n (%)	52 (23.1)	22 (16.1)	30 (34.1)	**0.002**
STS score	9.5±3.2	10±3.2	8.8±3.2	0.006
Hemoglobine (g/dL)	11.4±1.7	11.3±1.7	11.3±1.6	0.831
Albumin (g/dL)	3.66±0.46	3.62±0.45	3.71±0.49	0.188
Creatinine (mg/dL)	1.0 (0.8-1.3)	1.0 (0.8-1.3)	1.0 (0.8-1.3)	0.147
e-GFR (mL/min)	64.3±24	63.8±25.6	65.1±21.5	0.689
LVEF (%)	53.8±11.3	54.1±10.9	53.7±12.1	0.784
AVA, cm^2	0.75±0.14	0.77±0.14	0.72±0.13	**0.024**
Mean aortic gradient (mm/Hg)	49.4±12.7	49.9±12.8	48.5±12.5	0.415
Valve type (self-expandable), n (%)	65 (28.9)	41 (29.9)	24 (27.3)	0.668
Valve size (mm)	26 (25-29)	26 (25-29)	26 (23-29)	0.105

AVA: Aortic valve area, CKD: Chronic kidney disease, COPD: Chronic obstructive pulmonary disease, CVD: Cerebrovascular disease, GFR: Glomerular filtration rate, HP: Hyperpolypharmacy, LVEF: Left ventricular ejection fraction, PAD: Peripheral artery disease, STS: Society of thoracic surgeons

that advanced age, hyperlipidemia, low left ventricular ejection fraction (LVEF), low hemoglobin levels, low AVA, and HPP were associated with 30-day mortality. Using the parameters that were significant in the univariate analysis, we conducted multivariate logistic regression analysis, which identified hemoglobin <10.1, LVEF <60%, low AVA, and HPP as independent predictors of 30-day mortality in TAVI patients (Table 4).

A comparison of medication burden based on the presence of 30-day mortality in patients with TAVI is depicted in Figure 2. Patients with 30-day mortality had a mean of 14 drugs, whereas those without had a mean of 9 drugs (p<0.001).

Discussion

The main finding of the present study was that HPP, defined as the use of at least 10 drugs, emerged as a significant independent predictor of 30-day mortality in patients undergoing TAVI. In addition, low hemoglobin levels, low LVEF, and lower AVA were independent predictors of 30-day mortality following TAVI. The prevalence of polypharmacy and HPP in the study population was 91% and 39.1%, respectively.

Our study revealed a high prevalence of polypharmacy and HPP, with rates of 91% and 39.1%, respectively. HPP, which is characterized by the use of at least 10 drugs according to geriatric literature (14), is a severe form of polypharmacy that has been linked to adverse outcomes such as disability, hospitalizations, and mortality (9). In defining polypharmacy, various criteria for drug classification exist, with the Anatomical Therapeutic Chemical and Multum classifications being commonly used. For instance, Unlu et al. (11) used the Multum classification in a study that examined the impact of polypharmacy in patients with HF. Given the high prevalence of cardiovascular comorbidities (such as coronary artery disease and HF) among patients with TAVI, the Multum classification used by Unlu et al. (11) may hold greater relevance.

Table 2. Medication profile based on hyperpolypharmacy

Variables	Total (n=225)	Non-HPP (-) (n=137)	HPP (+) (n=88)	p-value
Total medication count, mean (SD)	9 (7-12)	7 (5.5-9)	12 (11-14)	<0.001
Heart failure medications				
Beta blockers, n (%)	193 (85.8)	111 (82.2)	82 (91.1)	0.061
ACEI/ARB, n (%)	141 (62.7)	66 (48.9)	75 (83.3)	<0.001
MRA, n (%)	18 (8.0)	8 (5.9)	10 (11.1)	0.160
Vasodilators, n (%)	24 (10.7)	4 (3.0)	20 (22.2)	<0.001
Diuretics, n (%)	132 (58.7)	59 (43.7)	73 (81.1)	<0.001
Digoxin, n (%)	22 (9.8)	4 (3.0)	18 (20.0)	<0.001
Other cardiovascular agents				
Lipid lowering, n (%)	109 (48.4)	48 (35.6)	61 (67.8)	<0.001
Antiplatelets, n (%)	171 (76.0)	107 (79.3)	64 (71.1)	0.161
Anticoagulants, n (%)	48 (21.3)	20 (14.8)	28 (31.1)	0.003
Antiarrhythmics, n (%)	14 (6.2)	5 (3.7)	9 (10.0)	0.055
Calcium channel blockers n (%)	111 (49.3)	46 (34.1)	65 (72.2)	<0.001
Anti-anginal agents, n (%)	37 (16.4)	7 (5.2)	30 (33.3)	<0.001
Other antihypertensives, n (%)	50 (22.2)	15 (11.1)	35 (38.9)	<0.001
Non-cardiovascular medications				
Opioids, n (%)	40 (17.9)	13 (9.6)	27 (30.3)	<0.001
Non-opioid analgesics, n (%)	95 (42.2)	40 (29.6)	55 (61.1)	<0.001
Benzodiazepine, n (%)	22 (9.8)	6 (4.4)	16 (17.8)	<0.001
Antidepressants, n (%)	86 (38.2)	33 (24.4)	53 (58.9)	<0.001
Antipsychotics, n (%)	13 (5.8)	3 (2.2)	10 (11.1)	0.007
Anti-diabetics, n (%)	93 (41.3)	53 (39.3)	40 (44.4)	0.439
Antacids, n (%)	132 (58.9)	63 (46.7)	69 (77.5)	<0.001
Thyroid agents, n (%)	80 (35.6)	30 (22.2)	50 (55.6)	<0.001
Bronchodilators, n (%)	130 (57.8)	79 (58.5)	51 (56.7)	0.783
GU tract agents, n (%)	52 (23.1)	16 (11.9)	36 (40.0)	<0.001
Minerals/vitamins, n (%)	90 (40.0)	35 (25.9)	55 (61.1)	<0.001
Anti-infective agents, n (%)	66 (29.3)	24 (17.8)	42 (46.7)	<0.001
Anti-neoplastic agents, n (%)	14 (6.2)	4 (3.0)	10 (11.1)	<0.001
Topical agents, n (%)	90 (40.0)	35 (25.9)	55 (66.1)	<0.001

ACEI: Angiotensin-converting enzyme inhibitors, ARB: Angiotensin II receptor antagonists, GU: Genitourinary, MRA: Mineralocorticoid receptor antagonists, HPP: Hyperpolypharmacy, SD: Standard deviation

Risk assessment before surgical or transcatheter treatment is recommended in geriatric patients with severe AS (15). Frailty measurement is of great importance in this assessment and is effective in determining the prognosis of patients after the procedure. The multidimensional prognostic index (MPI) is recommended as a parameter to be used before the procedure and in long-term follow-up (16). MPI includes the number of drugs used, and the use of ⩾7 drugs is defined as a serious drug burden (17). Previous studies have reported a negative correlation between increased medication burden and functional capacity, which directly affects the prognosis of patients with TAVI (18,19,20). The Charlson Comorbidity Index (CCI) is a widely used measure of frailty that is associated with polypharmacy (21). George et al. (22) conducted a study that found CCI to be correlated with 30-day mortality and VARC-2 outcomes in patients undergoing TAVI. Additionally, the literature has reported a negative correlation between increased medication burden and functional capacity, which directly impacts the prognosis of TAVI patients (23).

These findings are supported by our study, which suggests that polypharmacy is a significant indicator of frailty and is associated with adverse clinical outcomes and 30-day mortality in patients with TAVI. Our study underscores the importance of conducting a thorough geriatric and frailty assessment in patients with TAVI to optimize their care.

The relationship between polypharmacy and adverse events in patients undergoing TAVI cannot be elucidated through a unifying mechanism. Utilization of multiple medications primarily arises from comorbidities associated with multiple diseases, representing a pivotal determinant influencing unfavorable outcomes (24). Polypharmacy is intricately linked to various mechanisms. Notably, drug-drug interactions constitute a significant facet of this relationship. The interplay among diverse pharmacological agents can induce alterations in their plasma concentrations, accentuating harmful aspects of their effects or side effects, thereby precipitating instances of bleeding and cognitive impairment among patients (24). Concurrently, heightened instances of medication non-adherence and administration errors engender therapeutic dissociation, impeding optimal treatment outcomes. Furthermore, the decline in cognitive functions, which frequently results in fall incidents, has emerged as a substantial contributor to mortality, particularly in the elderly population (25). The combination of these complexities, along with other factors related to taking multiple medications after TAVI, increases the possibility of negative events. We believe that the combination of more bleeding, higher chances of falls, increased vulnerability to infections, and cognitive problems, along with longer stays in intensive care and the hospital, contribute to the higher mortality rates in this group. Indeed, the high rate of 30-day mortality in the polypharmacy group, as well as the elevated incidence of major bleeding, can be explained through these mechanisms in our study. Furthermore, a study examining the relationship between the frailty index, which includes polypharmacy, and major bleeding in patients with TAVI also supports this finding (26). Therefore, optimizing the number of drugs and preventing unnecessary prescribing are of critical importance in patients with TAVI.

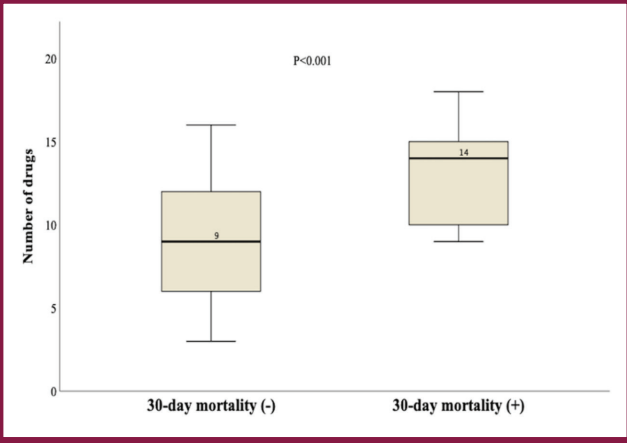

Figure 2. Comparison of medication burden according to the presence of 30-day mortality in TAVI patients
TAVI: Transcatheter aortic valve implantation

Study Limitations

This study has some limitations, such as its retrospective and single-center nature, which may limit the generalizability of the findings. Furthermore, various parameters for frailty assessment, including albumin levels, sarcopenia, and the CCI, were not incorporated into the study design. The study did not consider post-procedure management, which could have had an impact on both 30-day mortality and clinical outcomes. In addition, the medication count did not consider combination pills containing multiple pharmacologically active ingredients, and drug dosages were not fully determined. These limitations should be considered in future research. Finally, angiotensin receptor-neprilysin inhibitors were not included in the study, and sodium-glucose cotransporter 2 inhibitors, which are now considered HF drugs, were evaluated in the antidiabetic medication group.

Table 3. Clinical outcomes of patients based on hyperpolypharmacy

Variables	Total (n=225)	Non-HPP (-) (n=137)	HPP (+) (n=88)	p-value
30-day mortality	10 (4.4)	2 (1.5)	8 (8.9)	**0.016**
Stroke	7 (3.1)	4 (3)	3 (3.3)	0.875
Major bleeding	32 (14.2)	11 (8.1)	21 (23.3)	**<0.001**
AKI	41 (18.2)	20 (14.8)	21 (23.3)	0.105
Major vascular complications	15 (6.7)	3 (2.2)	12 (13.3)	**<0.001**
Pacemaker	21 (9.3)	12 (8.9)	9 (10)	0.779
MI	5 (2.2)	2 (1.5)	3 (3.3)	0.391

AKI: Acute kidney injury, MI: Myocardial infarction, HPP: Hyperpolypharmacy

Table 4. Logistic regression analysis of 30-day mortality

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age, years	1.092 (0.985-1.210)	**0.094**	1.174 (0.955-1.510)	0.173
Gender (male)	1.439 (0.362-5.720)	0.606		
Hypertension	1.056 (0.265-4.211)	0.938		
Previous cardiac surgery	1.491 (0.371-5.987)	0.573		
Coronary artery disease	0.962 (0.264-3.510)	0.953		
COPD	1.648 (0.415-6.548)	0.478		
Diabetes mellitus	0.607 (0.153-2.410)	0.478		
Hyperlipidemia	1.899 (0.901-4.002)	**0.092**	1.978 (0.805-4.561)	0.211
CKD	1.441 (0.394-5.274)	0.581		
PAD	0.888 (0.223-3.537)	0.866		
CVD	3.048 (0.912-9.124)	0.167		
Atrial fibrillation	2.319 (0.629-8.555)	0.206		
STS score	1.018 (0.845-1.226)	0.855		
Hemoglobine	0.549 (0.343-0.879)	**0.013**	0.478 (0.268-0.899)	**0.017**
Albumin	0.882 (0.228-3.413)	0.856		
Creatinine	0.990 (0.318-3.082)	0.986		
e-GFR	0.988 (0.961-1.017)	0.418		
LVEF	0.937 (0.892-0.983)	**0.008**	0.934 (0.864-0.988)	**0.018**
AVA	0.004 (0.000-0.399)	**0.019**	0.020 (0.000-4.010)	0.165
Mean aortic gradient	1.001 (0.952-1.052)	0.970		
Valve type (self-expandable)	2.583 (0.722-9.244)	0.145		
Valve size	0.984 (0.800-1.211)	0.811		
Hyperpolypharmacy	6.488 (1.345-31.301)	**0.020**	5.42 (1.187-28.549)	**0.041**

AVA: Aortic valve area, CKD: Chronic kidney disease, COPD: Chronic obstructive pulmonary disease, CVD: Cerebrovascular disease, GFR: Glomerular filtration rate, HPP: Hyperpolypharmacy, LVEF: Left ventricular ejection fraction, PAD: Peripheral artery disease, STS: Society of thoracic surgeons, OR: Odds ratio, CI: Confidence interval

Conclusion

In summary, the present study provides evidence that HPP, defined as the use of at least 10 drugs, is prevalent among patients undergoing TAVI and is associated with unfavorable clinical outcomes. The coexistence of polypharmacy, frailty, and multiple comorbidities in the elderly necessitates appropriate prescribing practices and medication management strategies to prevent adverse events. Therefore, clinicians should increase their awareness of this issue and strive to reduce unnecessary drug use to mitigate the negative impact of polypharmacy. The results of our study highlight the importance of geriatric assessment in patients with TAVI, particularly for identifying HPP, as it plays a crucial role in predicting adverse outcomes.

Ethics

Ethics Committee Approval: The study protocol was approved by the University of Health Sciences Türkiye, Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital Ethics Committee in April 2021 (decision no: 2021/38, date: 27.04.2021), and the study was conducted in accordance with the principles outlined in the Declaration of Helsinki.

Informed Consent: Retrospectively study.

Authorship Contributions

Surgical and Medical Practices: A.K.K., M.E., Concept: S.A., G.B.G., Design: İ.G., Data Collection or Processing: S.T.K, A.D., G.D., Analysis or Interpretation: M.A., A.R.D., Literature Search: S.A., Writing: A.G.

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