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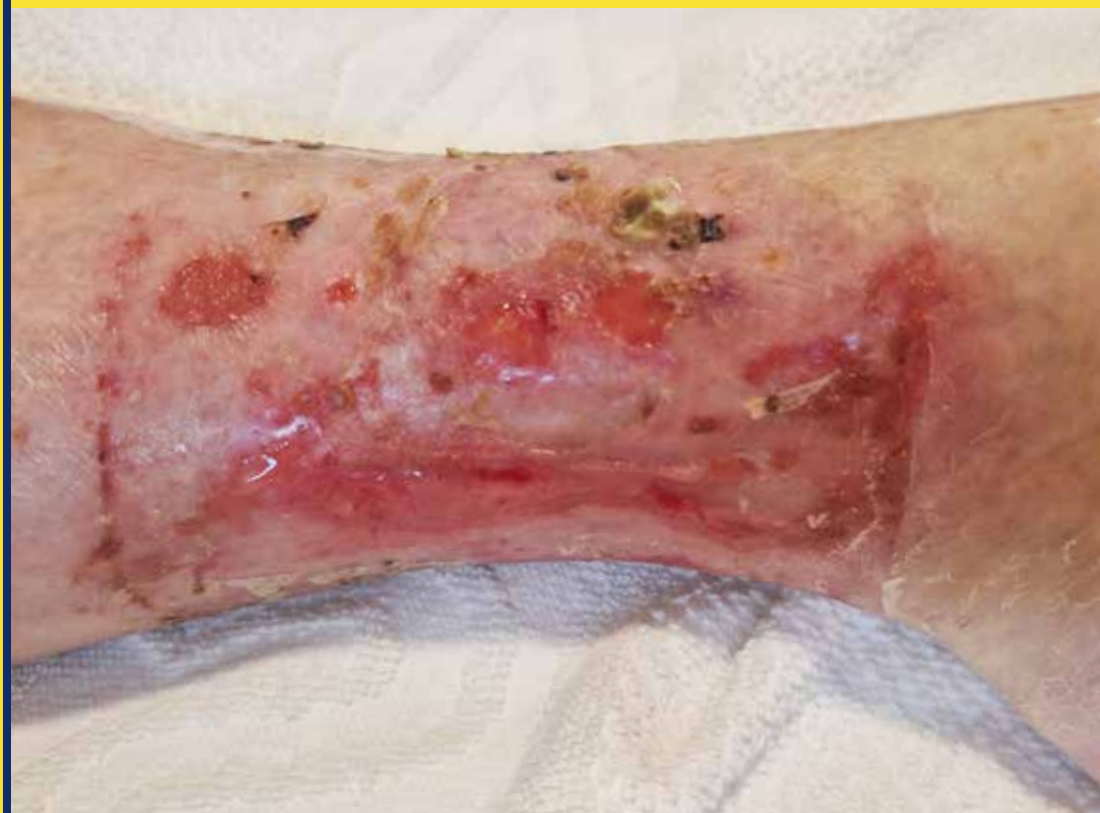
ACTA MEDICO-BIOTECHNICA



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35. posvet Medicina, pravo in družba, 26. 3. 2026, Univerza v Mariboru

Spoštovani člani organizacijskega odbora mednarodnega posveta, predavatelji, moderatorji in razpravljavci, cenjeni visoki gostje, drage študentke in študenti, gospe in gospodje!

Zdravje je ena najglobljih in hkrati najbolj univerzalnih vrednot človeštva. Ko je ogroženo zdravje, postanejo nepomembne razlike med državami, kulturami ali družbenimi sistemi. Ostane le skupna človeška izkušnja ranljivosti in potreba po solidarnosti. Prav zato vprašanja zdravja vedno presegajo meje medicine in postajajo tudi vprašanja prava, etike, družbe in globalne odgovornosti.

V veliko čast mi je in v iskreno zadovoljstvo, da vas lahko pozdravim na 35. jubilejni mednarodni konferenci Medicina, pravo in družba.

Petintrideset let kontinuiranega strokovnega dialoga je pomemben dosežek. Hkrati pa je tudi dokaz, da so vprašanja na stičišču medicine, prava in družbe danes morda še pomembnejša, kot so bila ob začetkih te konference. Svet, v katerem živimo, postaja vse bolj povezan, hkrati pa tudi vse bolj kompleksen. Prav zato potrebujemo prostor dialoga, v katerem se srečujejo različna znanja, izkušnje in perspektive.

Tema letošnje konference »Trajnostni razvoj zdravstva« odpira eno ključnih vprašanj sodobnega časa: kako zagotoviti zdravstvene sisteme, ki bodo dostopni, pravični in vzdržni tudi za prihodnje generacije?

Zdravje danes ni več zgolj medicinsko vprašanje. Postaja tudi pravno, etično, družbeno in globalno vprašanje. Podnebne spremembe, demografski premiki, migracije, nove nalezljive bolezni ter socialne neenakosti pomembno vplivajo na zdravje ljudi in na delovanje zdravstvenih sistemov. Dostop do

Address of the UM Rector Full Professor Zdravko Kačič

35th Conference Medicine, Law and Society, March 26, 2026, University of Maribor

Revered members of the organizational committee of the international conference,
lecturers, moderators and scientific discussants, esteemed distinguished guests, dear students, ladies and gentlemen!

Health is one of the most profound and one of the most universal values of humanity. When health is jeopardised, the differences between countries, cultures or social systems become unimportant. What remains is only common human experience of vulnerability and the need for solidarity. This is exactly why issues of health always surpass the frames of medicine and are also becoming issues of law, ethics, society and global responsibility.

Therefore, it is my great honour and sincere pleasure to welcome you to the 35th anniversary of the international conference Medicine, Law and Society.

Thirty-five years of continual professional dialogue is an important achievement. Simultaneously, it is also proof that issues at the intersection of medicine, law and society are today perhaps even more important than they were when this conference was first held. The world we live in is becoming ever more connected, and at the same time ever more complex. This is the reason we need a space for dialogue in which various forms of knowledge, experiences and perspectives meet.

The theme of this year's conference "Sustainable Development of Healthcare" is one of the key issues of contemporary time: how to ensure that healthcare systems will be accessible, just and sustainable for future generations.

Health nowadays is no longer merely a medical issue. It is also becoming a legal, ethical, social and global issue. Climate changes, demographic shifts, migrations, new

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zdravstvene oskrbe zato postaja eno temeljnih meril pravične in solidarne družbe.

Že Hipokrat je opomnil, da mora v središču vsakega zdravstvenega sistema vedno biti človek, njegova ranljivost, njegovo dostojanstvo in njegova pravica do oskrbe. Vse to je izpostavil v misli, ki je po skoraj tisočletju in pol še vedno aktualna: »*Kjer je ljubezen do človeka, tam je tudi ljubezen do medicine.*«.

Ko razmišljamo o prihodnosti zdravstva, je prav, da v zvezi s tem upoštevamo tudi pomembne zgodovinske mejnike. Leta 1948 je bila ustanovljena Svetovna zdravstvena organizacija ter sprejeta Splošna deklaracija človekovih pravic, ki je prvič jasno zapisala, da ima vsak človek pravico do življenjskega standarda, ki zagotavlja zdravje in dobrobit. Ti dokumenti so postavili temelje sodobnemu razumevanju zdravja kot temeljne človekove pravice.

Trajnost zdravstva ne pomeni le finančne stabilnosti sistemov; pomeni tudi trajnost solidarnosti, odgovornosti in zaupanja. To pa so vrednote, brez katerih noben zdravstveni sistem ne more delovati dolgoročno.

Poseben izziv našega časa predstavlja tudi hiter razvoj umetne inteligence in digitalnih tehnologij v zdravstvu. Napredni algoritmi danes pomagajo pri zgodnjem odkrivanju bolezni, izboljšujejo diagnostične postopke in omogočajo bolj personalizirano zdravljenje. Digitalne rešitve lahko pomembno prispevajo k večji dostopnosti zdravstvenih storitev.

A tehnološki napredek vedno odpira tudi nova vprašanja. Gre za vprašanja odgovornosti, varovanja zasebnosti, pravičnosti in zaupanja. In tehnologija sama po sebi ni odgovor. Odgovor je vedno človek s svojo etiko, odgovornostjo in zavezanostjo k skupnemu dobremu.

Zato so razprave o bioetičnih in eksistencialnih izzivih sodobne medicine danes pomembnejše, kot kdaj koli prej. Zdravnik, teolog in humanist Albert Schweitzer je zapisal:

»*Humanost ni v tem, da živimo bolje od drugih, temveč da živimo za druge.*«.

Ta misel zelo jasno povzema bistvo poslanstva zdravstva, prav tako pa tudi poslanstva univerz.

Univerze niso le ustanove znanja. So tudi prostori odgovornosti za prihodnost družbe. Na univerzah

infectious diseases and social inequalities have a vital influence on people's health and on the functioning of healthcare systems. Access to healthcare is therefore becoming one of the basic criteria of a just and solidary society.

Hippocrates reminded us that at the centre of each healthcare system there is a human being, his or her vulnerability, dignity and right to health. All of this he put forward in his thought which is after almost a millennium and a half still relevant: "*Where there is love for humanity, there is also love for medicine.*"

When thinking about the future of healthcare, it is also right to remember vital historical milestones. In the year 1948, the World Health Organization was established and the Universal Declaration of Human Rights was adopted which for the first time it was clearly written down that every human has the right to a standard of living which assures health and welfare. These documents have laid the foundations for the modern understanding of health as a fundamental human right.

Sustainability of healthcare does not only mean the financial stability of systems. It also means sustainability of solidarity, responsibility and trust. These are values without which no healthcare system can operate in the long term.

A special challenge of our times is the rapid development of artificial intelligence and digital technologies in healthcare. Advanced algorithms currently help in early detection of diseases, improve diagnostic procedures and facilitate more personalized treatment. Digital solutions can also contribute to greater accessibility of health services.

However, technological progress also raises novel issues, such as responsibility, privacy protection, justice and trust. Thus, technology by itself is not the answer. The answer is always a human with his or her ethics, responsibility and commitment to the common good.

This is why discussions about the bioethical and existential challenges of modern medicine are more vital than ever before. A physician, theologian, and humanist Albert Schweitzer wrote: "*Humanity is not about living better than others, but about living for others.*"

This thought very clearly summarizes the essence

nastajajo nova znanja, nove ideje in nove generacije strokovnjakov, ki bodo oblikovale zdravstvene sisteme, pravne okvire in družbene politike prihodnosti.
Na Univerzi v Mariboru se te odgovornosti dobro zavedamo. Zato si prizadevamo za raziskovanje in izobraževanje, ki prispevata k razvoju družbe, k boljšemu zdravju ljudi ter k spoštovanju temeljnih humanističnih vrednot.
Spoštovani. Konference, kot je ta, imajo izjemno vrednost. So prostor srečevanja idej, strok in kultur. Prav v takšnih srečanjih nastajajo nova partnerstva, nova razumevanja in pogosto tudi nove rešitve za kompleksne izzive našega časa.
Prepričan sem, da bodo razprave na tej konferenci pomembno prispevale k razmisleku o tem, kako lahko skupaj gradimo bolj pravične, dostopne in trajnostne zdravstvene sisteme.
Dovolite mi, da ob koncu izrečem še misel, ki nas naj spremlja tudi v prihodnje;
trajnost zdravstva ni le vprašanje sistemov, tehnologij ali zakonodaje, temveč je v svojem bistvu vedno vprašanje naše skupne odgovornosti za človeka.
Naj bo tudi ta konferenca korak v tej smeri!
Hvala lepa.

Prof. dr. Zdravko Kačič,
rektor Univerze v Mariboru

of the mission of healthcare and the mission of universities as well.
Universities are not only institutions of knowledge. They are also premises of responsibility for the future of society. Universities produce new knowledge, new ideas, and new generations of experts who will shape healthcare systems, legal frameworks, and social policies of the future.
At the University of Maribor we are highly aware of this responsibility. That is why we strive for research and education which contribute to the development of society, to improve the health of people and to respect fundamental humanistic values.
Revered guests, conferences like this one have exceptional value. They are a meeting place for ideas, professions, and cultures. It is in such meetings that new partnerships, new understandings and often new solutions are created for complex challenges of our times.
I am convinced that discussions at this conference will vitally contribute to reflection on how we can together build more just, accessible, and sustainable healthcare systems.
Allow me to conclude with a thought that may accompany us in the future: sustainability of healthcare is not only an issue of systems, technologies or legislation, but at its core it is always an issue of our joint responsibility for humanity.
Let this conference be a step in this direction.
Thank you very much.

Full Professor Zdravko Kačič,
Rector of the University of Maribor

Koristi in pasti zdravljenja s SGLT-2 zaviralci

Balancing the Benefits and Risks of SGLT2 Inhibitors

Avtor / Author

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Izvleček

Srčnožilne, ledvične in presnovne bolezni so eden izmed vodilnih vzrokov obolevnosti in umrljivosti po svetu. Zaviralci natrij–glukoznega kotransporterja 2 (angl. sodium-glucose cotransporter-2 inhibitors, SGLT2i) so izkazali pomembne koristi, ki presegajo zgolj uravnavanje glikemije. V preglednem članku so obravnavani trenutno dostopni dokazi o ledvičnih, srčnožilnih in presnovnih učinkih SGLT2i s poudarkom na ključnih kliničnih raziskavah o njihovi uporabi.

Z zaviranjem ponovnega privzema natrija in glukoze v proksimalnem ledvičnem tubulu SGLT2i ponovno vzpostavijo tubuloglomerularno povratno zanko, zmanjšajo intraglomerularni tlak in zmanjšajo glomerularno hiperfiltracijo, s čimer upočasnijo napredovanje kronične ledvične bolezni. Večje randomizirane kontrolirane raziskave so pokazale

Abstract

Cardiovascular, renal, and metabolic diseases frequently coexist and are leading contributors to global morbidity and mortality. Sodium–glucose cotransporter 2 inhibitors (SGLT2is), originally developed for the treatment of type 2 diabetes mellitus, have demonstrated substantial benefits extending beyond glycemic control. This review synthesizes current evidence on the renal, cardiovascular, and metabolic effects of SGLT2is and highlights key clinical outcome trials supporting use.

SGLT2is restore tubuloglomerular feedback, reduce intraglomerular pressure, and attenuate glomerular hyperfiltration by inhibiting sodium–glucose reabsorption in the proximal renal tubule, thereby slowing the progression of chronic kidney disease. Large randomized controlled trials have consistently

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zmanjšanje števila hospitalizacij zaradi srčnega popuščanja ter zmanjšanje srčnožilne umrljivosti, in to tudi pri populacijah brez sladkorne bolezni. Poleg tega imajo SGLT2i številne ugodne metabolne sistemske učinke, vključno z zmernim zmanjšanjem telesne teže in krvnega tlaka, izboljšano presnovno učinkovitostjo, ter tudi modulacijo vnetja in oksidativnega stresa.

V obravnavo so prav tako zajeti neželeni učinki, vključno z genitourinarnimi okužbami, hipovolemijo, prehodnim poslabšanjem ledvične funkcije ter redkimi zapleti, kot sta diabetična ketoacidoza in Fournierjeva gangrena.

demonstrated reductions in kidney disease progression, hospitalization for heart failure, and cardiovascular mortality in populations with and without diabetes. In addition, SGLT2is exert systemic effects, including modest reductions in body weight and blood pressure, improved metabolic efficiency, and modulation of inflammatory and oxidative stress pathways.

Adverse effects, including genitourinary infections, volume depletion, transient declines in renal function, and rare events, such as diabetic ketoacidosis and Fournier's gangrene, are also discussed.

In summary, SGLT2is represent a transformative therapeutic strategy with broad, multi-system benefits across cardiovascular, renal, and metabolic diseases.

INTRODUCTION

Chronic kidney disease (CKD), type 2 diabetes (T2D), and cardiovascular disease (CVD) are major contributors to global morbidity and premature mortality. Cardiovascular–renal–metabolic (CRM) syndrome describes the interconnected dysfunction of these systems, leading to multiorgan and cardiovascular complications. CRM syndrome is often driven by excess or dysfunctional visceral adipose tissue, which releases proinflammatory and pro-oxidative mediators that promote vascular, cardiac, and renal injury and impair insulin sensitivity (1, 2). The 1999–2020 NHANES data indicated that ~25% of individuals have at least 1 CRM condition with multimorbidity affecting 8% overall and 25% of adults ≥ 65 years. The burden increases with age and is associated with male gender, Black race, adverse socioeconomic factors, and a higher prevalence of T2D, obesity, physical inactivity, and uncontrolled hypertension (2).

Sodium-glucose cotransporter 2 inhibitors (SGLT2is), also known as gliflozins, are oral antidiabetic drugs that act by selectively blocking the SGLT2 cotransporter in the S1 segment of the proximal renal tubule, thereby preventing glucose and sodium reabsorption. This mechanism results in sustained glucosuria and natriuresis and is associated with clinically relevant reductions in glycated hemoglobin (HbA1c), body weight, blood pressure, and albuminuria (3).

SGLT2is provide cardiovascular and renal protection, even in non-diabetic patients. SGLT2is are now a central therapy for heart failure and CKD. Additional benefits include modest weight loss and blood pressure reduction via natriuresis, although monitoring for adverse effects remains essential (3-6).

This review discusses the effects of SGLT2is and summarizes the key landmark clinical trials evaluating use. The therapeutic benefits and potential adverse effects associated with treatment are highlighted. Crucial steps in prescribing SGLT2is are presented in Figure 1.

BENEFICIAL EFFECTS OF SGLT2IS

Renoprotective effects

SGLT2is protect the kidney by restoring tubuloglomerular feedback, reducing intraglomerular pressure, and reversing hyperfiltration, thereby stabilizing filtration and slowing CKD progression (6-15). An initial glomerular filtration rate (GFR) reduction is later followed by long-term GFR

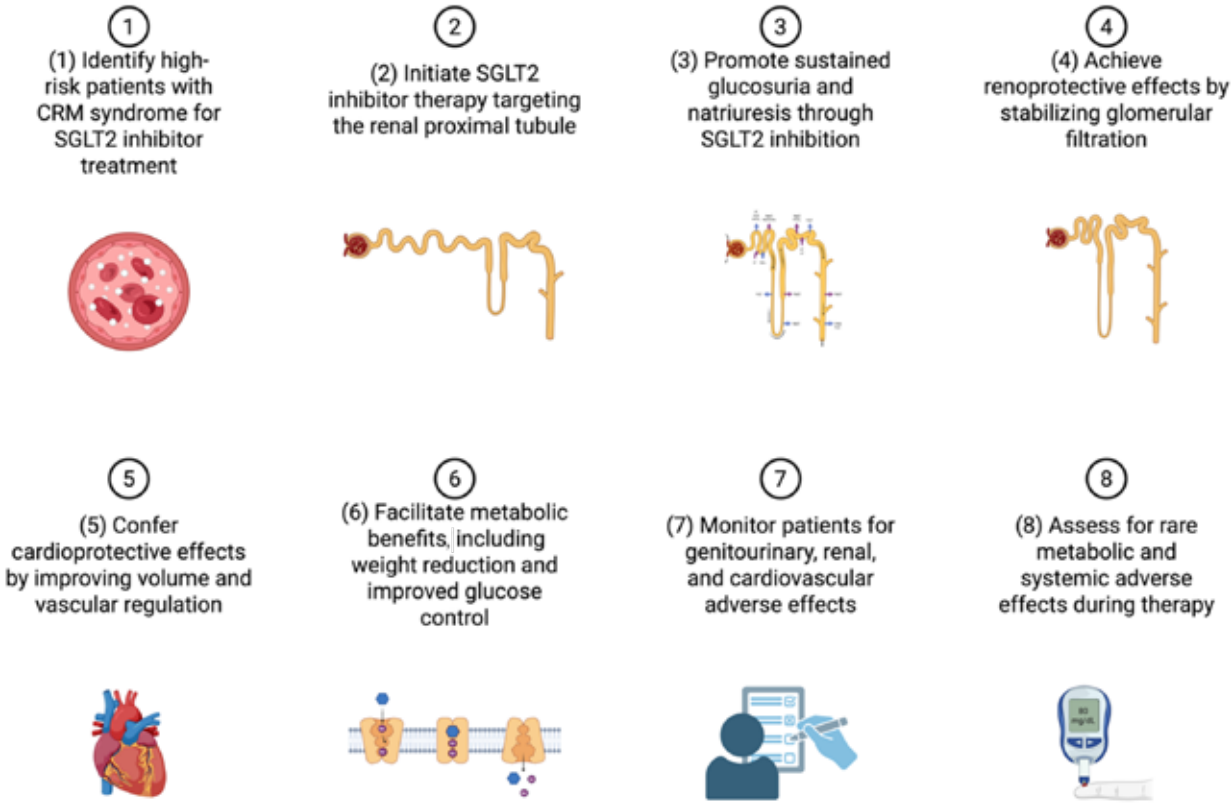

Figure 1. *Crucial steps in prescribing sodium-glucose cotransporters-2.*

Legend: CRM – cardiorenal and metabolic syndrome, SGLT2 – sodium-glucose cotransporter-2

preservation and a reduced risk of developing acute kidney injury (16).

Dapagliflozin reduced the risk of renal composite outcomes compared to placebo (HR = 0.76) in DECLARE–TIMI 58 (10). Empagliflozin significantly lowered the risk of kidney disease progression or cardiovascular death in EMPA-KIDNEY across a broad range of baseline eGFRs, including patients with advanced CKD (12). Canagliflozin reduced the risk of progression to end-stage kidney disease in the CREDENCE trial by 32% compared to placebo [HR = 0.68] (13). These hemodynamic improvements are accompanied by marked reductions in albuminuria and proteinuria, reflecting a strengthened glomerular filtration barrier and reduced tubular stress. Such changes reflect the combined effects of lower intraglomerular pressure, which reduces epithelial sodium channel (EnaC)-mediated sodium retention and consequently limits injury to distal tubular segments (8, 10-13, 17-22). In addition to the hemodynamic effect, SGLT2 inhibition improves renal oxygenation and mitochondrial efficiency, reduces tubular ATP demand, activates autophagy pathways, and attenuates oxidative and inflammatory stress, thereby protecting nephron integrity under metabolic and hypoxic load (6, 7, 9, 19, 21-25). Clinically, these changes manifest as consistently lower rates of acute kidney injury (AKI), including severe episodes requiring hospitalization, and preserved kidney function, even in patients with

advanced CKD or a markedly reduced eGFR (3, 10-15, 26, 27).

Cardioprotective effects

SGLT2is confer consistent cardiovascular protection through integrated hemodynamic, vascular, and anti-inflammatory mechanisms. SGLTis lower cardiac preload and afterload, stabilize volume status, and reduce systolic and diastolic blood pressure by inducing natriuresis and osmotic diuresis without compensatory tachycardia (10-15, 17, 23). These blood-pressure–lowering effects were modest but consistent across landmark outcome trials. Dapagliflozin reduced systolic blood pressure by 2.7 mm Hg (95% CI = 2.4–3.0 mmHg) and diastolic blood pressure by 0.7 mmHg (95% CI = 0.6–0.9 mmHg) in DECLARE–TIMI 58 compared to placebo (10). Empagliflozin was associated with reductions of 2.6 ± 0.3 mmHg in systolic and 0.5 ± 0.2 mmHg in diastolic blood pressure in EMPA-KIDNEY (12), while canagliflozin lowered systolic blood pressure by 3.30 mmHg (95% CI = 2.73–3.87) and diastolic blood pressure by 0.95 mm Hg (95% CI = 0.61–1.28) in CREDENCE relative to placebo (13). These hemodynamic effects translated into fewer hospitalizations for heart failure and reductions in cardiovascular mortality across a broad range of patients. Dapagliflozin reduced the composite of cardiovascular death or hospitalization for heart failure (HR = 0.83) but did not significantly reduce cardiovascular death alone (HR = 0.98) in DECLARE–TIMI 58 (10). Empagliflozin significantly reduced death from cardiovascular causes with no significant differences in myocardial infarction or stroke compared to placebo in EMPA-REG OUTCOME (11). Cardiovascular outcomes in EMPA-KIDNEY were consistent with prior evidence. Specifically, pooled analyses showed a 14% reduction in cardiovascular mortality (RR = 0.86) and a 23% reduction in hospitalization for heart failure or cardiovascular death (RR = 0.77) in EMPA-KIDNEY (12). Canagliflozin reduced the risk of cardiovascular death, myocardial infarction, or stroke (HR = 0.80; 95% CI = 0.67–0.95) and substantially lowered the hospitalization rate for heart failure (HR = 0.61; 95% CI = 0.47–0.80) in CREDENCE compared to placebo (13). Improvements in vascular compliance, endothelial function, and arterial stiffness further reduce cardiac workload and enhance circulatory stability (10-15). Additional cardioprotective mechanisms include attenuation of oxidative stress, reduced inflammatory signaling, and improved mitochondrial homeostasis, which together reduce ischemia–reperfusion injury and limit post-MI remodeling (15, 28). Broader clinical benefits include reductions in major adverse cardiovascular events, fewer recurrent heart-failure episodes, decreased need for loop-diuretic therapy, and improved outcomes in non-diabetic populations with pooled analyses demonstrating lower all-cause and cardiovascular mortality (3, 11, 14). Importantly, these cardiovascular benefits occur independent of glycemic control, reflecting the consistency across different SGLT2is (10-15).

Metabolic and other systemic favorable effects

SGLT2is also exert a broad set of metabolic benefits primarily through insulin-independent glucosuria (10-13). Urinary glucose loss creates a caloric deficit and leads to modest weight reduction. Dapagliflozin reduced body weight by 1.8 kg in DECLARE–TIMI 58 compared to placebo (10). Empagliflozin resulted in a mean decrease in body weight of 0.9 ± 0.1 kg during follow-up in the EMPA-KIDNEY trial (12). Similarly, canagliflozin therapy led to a reduction in body weight of 0.80 kg (95% CI = 0.69–0.92) in the CREDENCE trial relative to placebo (13). Natriuresis and osmotic diuresis represent central systemic mechanisms that improve sodium–water balance and reduce fluid overload, while maintaining stable volume status in patients without pre-existing fluid overload (8, 10-15). Additional systemic effects include reductions in serum uric acid (10-14), a favorable shift in lipid profile (17), and a mild fasting-like metabolic state with enhanced ketone utilization (7, 9). SGLT2 inhibition promotes autophagy via mTOR suppression, preserves mitochondrial structure, reduces oxidative stress through NRF2 activation, and prevents apoptosis by modulating BAX/BCL-2 signaling at the cellular level (6, 21, 22, 24, 25). Improved mitochondrial oxygen efficiency, enhanced erythropoietin production, and

increases in hematocrit further support metabolic and oxygen-delivery capacity (7, 24). These mechanisms contribute to reduced all-cause mortality, fewer hospitalizations, and systemic stabilization in high-risk patients (3, 11, 12, 14, 16).

UNDESIRABLE EFFECTS OF SGLT2 INHIBITORS ON THE KIDNEYS

Urogenital tract

Genitourinary infections occur in 10%–15% of patients receiving SGLT2is, mainly due to glucosuria. While the risk of urinary tract infections is not consistently increased in patients receiving SGLT2is, genital infections are more common, particularly in women, patients with T2D, and patients with prior infections or predisposing conditions. These infections are usually mild-to-moderate and respond to standard treatment (3-5, 17, 23, 26, 28-30).

Fournier gangrene (FG) is a very rare but serious complication of SGLT2i treatment, occurring in 1.6 per 100,000 males (3.3 per 100,000 among males 50–79 years of age) and 0.25 per 100,000 in the US (31). FG is more common in males and patients with diabetes and other comorbidities, and is likely driven by bacterial growth in glucose-rich tissues and impaired immunity. Infections are typically polymicrobial and may follow local breaches, such as procedures or trauma (4, 18). Empagliflozin is associated with the highest number of FG reports, followed by canagliflozin and dapagliflozin. Among SGLT2is, the combination of empagliflozin and metformin had the strongest association with FG (1).

As the eGFR declines, the anti-hyperglycemic effect of SGLT2is diminishes, particularly when the eGFR falls below 30 mL/min/1.73 m². This finding may lead to fluctuations in renal function and in some cases to AKI. Risk factors for AKI include older age (≥ 65 years), pre-existing renal impairment, diuretic use, hypovolemia, infection, sepsis, or exposure to nephrotoxic agents (4, 17, 29).

There are reports indicating that among patients with advanced CKD, the anti-hyperglycemic effect of SGLT2is may be reduced, although the renal protective benefits are generally preserved (3, 7, 26, 28).

Early renal hemodynamic effects may be diminished by concurrent loop diuretic use or high dietary salt and protein intake, due to blunting of SGLT2-mediated tubuloglomerular TGF activation (24).

Many of these effects are transient, such as a decline in the eGFR due decreased glomerular hyperfiltration because of reduced intraglomerular pressure, which then typically stabilizes (23, 24, 26, 28). Temporary medullary hypoxia may also occur due to workload shifting to downstream segments until compensatory mechanisms (hypoxia-inducible factor [HIF]-erythropoietin [EPO] pathway) restore balance (7), which can result in AKI. Tubulointerstitial nephritis (TIN), which requires a biopsy for diagnosis, is a rare drug-induced cause of AKI that may occur with SGLT2is. Recognition of TIN is important because TIN may require corticosteroid or immunosuppressive therapy (32, 33).

A possible association between dapagliflozin and bladder cancer has been noted, although SGLT2is are not linked to an overall increased cancer risk compared to other glucose-lowering therapies. Clinical guidance advises caution in patients with hematuria or a history of bladder cancer due to potential tumor-promoting concerns (4).

Cardiovascular adverse effects

SGLT2is can cause mild hypotension and hypovolemia due to volume depletion and diuretic-like effects, particularly in adults ≥ 65 years, patients with a baseline eGFR < 60 mL/min/1.73 m², or patients on diuretics (3, 8, 17, 18, 23, 28-30). This effect may increase fall risk and potentially lead to fractures, especially with canagliflozin. The proposed mechanisms underlying hypotension and hypovolemia include intravascular volume contraction and alterations in calcium, phosphate, and vitamin D homeostasis, which may reduce bone mineral density (4, 6, 24).

Careful monitoring is recommended in patients with ongoing ulcers, peripheral artery disease, neuropathy, a history of diabetic foot ulcers, or prior amputations given the uncertainty regarding the role of SGLT2is in amputation risk and conflicting evidence (4, 18).

Metabolic and other systemic adverse effects

SGLT2is can induce modest changes in lipid metabolism, including slight increases in LDL- and HDL-cholesterol. Canagliflozin has been associated with an elevated risk of hyperkalemia, particularly when combined with angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers. The effect is most pronounced in patients with renal impairment, necessitating close electrolyte monitoring during therapy initiation or adjustment (4).

SGLT2is are associated with an approximately three-fold increased risk of diabetic ketoacidosis (DKA), including euglycemic DKA, due to elevated ketone production, even when blood glucose levels are normal. The highest risk for DKA appears with canagliflozin, followed by empagliflozin and dapagliflozin. Risk is higher during fasting, acute illness, perioperative stress, or in insulin-treated patients and temporary discontinuation 3–4 days before surgery is recommended (4, 23, 29). The incidence of DKA in clinical trials of SGLT2is ranges from 0.2–2.2 events per 1000 patient-years in individuals with T2D, representing a 2.5-fold increase versus placebo. In type 1 diabetes, The risk may be 6–8-fold higher compared to placebo, with real-world incidence rates estimated at 43–71 events per 1000 patient-years (34).

Hypoglycemia is uncommon in patients treated with SGLT2is alone. The weighted incidence rate of hypoglycemia is 2.1 events per 100 person-years with SGLT2is and 0.6 events per 100 person-years for severe hypoglycemia (< 54 mg/dL [3.0 mmol/L]). Hypoglycemia may occur when combined with insulin or sulfonylureas without a dose adjustment (9,3). Moreover, the risk of hypoglycemia is lower with SGLT2is compared to sulfonylureas (35).

CONCLUSION

SGLT2is exert renal, cardiovascular, and metabolic benefits in addition to lowering glucose levels and reducing kidney disease progression, heart failure hospitalization, and cardiovascular mortality. The side effects associated with SGLT2is are generally well-tolerated, although monitoring for adverse effects is required.

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Diagnostika in zdravljenje demence v Zdravstvenem domu Radovljica – retrospektivna študija

Diagnostics and Treatment of Dementia in Radovljica Health Center – A Retrospective Study

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Izvleček

Namen: *Namen raziskave je bil preveriti, ali imajo bolniki z na novo diagnosticirano demenco opravljeno oceno kognitivnega stanja in katero diagnostično orodje je bilo za to uporabljeno. Prav tako smo preverili, če so opravili laboratorijsko in slikovno diagnostiko. Zanimalo nas je še, ali so jim zdravniki družinske medicine uvedli antidementiv ali jih napotili h kliničnemu specialistu (nevrologu ali psihiatru).*

Metode: *Opravljena je bila retrospektivna kvantitativna raziskava v Zdravstvenem domu Radovljica za opazovano obdobje od 1. 1. 2014 do 31. 12. 2018 z analizo njihove zdravstvene dokumentacije.*

Rezultati: *V raziskavo je bilo vključenih 98 bolnikov, od tega 28,6 % (n = 28) moškega in 71,4 % ženskega*

Abstract

Aim: *The aim of this study was to determine whether patients with newly diagnosed dementia underwent an assessment of cognitive status and which assessment tool was used. We also examined whether patients underwent laboratory and imaging diagnostics and investigated whether they were prescribed anti-dementia medication by their family physician or referred to a clinical specialist (neurologist or psychiatrist).*

Methods: *A retrospective quantitative study was conducted at the Radovljica Health Center, based on an analysis of patients' medical records from January 1, 2014, to December 31, 2018.*

Results: *The study included 98 patients, 28.6% males (n = 28) and*

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(n = 70) spola, starih od 75 do 96 let. V povprečju so imeli 3,7 kroničnih nenalezljivih bolezni, najpogosteje arterijsko hipertenzijo 81,6 % (n = 80) bolnikov in hiperlipidemijo 41,8 % (n = 41) bolnikov. Povprečno je imel obravnavan bolnik 4,2 rednih zdravil. Kognitivno stanje je bilo ocenjeno pri 19,4 % (n = 19) bolnikih, največkrat je bil uporabljen KPSS pri 89,5 % (n = 17) bolnikih; sledila sta TRU pri 5,3 % (n = 1) bolnikov in MocCA pri 5,3 % (n = 1) bolnikov. V letu diagnoze so bile opravljene laboratorijske preiskave pri 88,8 % (n = 87) bolnikov, od tega osnovne laboratorijske preiskave pri 65,3 % (n = 64) bolnikih. Na slikovno diagnostiko je bilo napotenih 25,5 % (n = 25) bolnikov. H kliničnem specialistu je bilo napotenih 79,6 % (n = 78) bolnikov, 28,6 % (n = 28) k psihiatru in 51,0 % (n = 50) k nevrologiji. Ob določitvi diagnoze demenca je bil pri 9,8 % (n = 10) uveden anitdementiv s strani zdravnika družinske medicine.

***Zaključek:** Ta raziskava je ugotovila, da pri diagnostiki in zdravljenju demence na primarnem nivoju obstaja prostor za izboljšavo obravnave (kognitivna ocena, laboratorijske preiskave, slikovna diagnostika). Predvsem pa je potreben napredek pri samostojnem uvajanju antidementiva s strani zdravnikov specialistov družinske medicine.*

71.4% females (n = 70), aged 75 to 96 years. Patients had average of 3.7 chronic non-communicable diseases, most commonly arterial hypertension (81.6%, n = 80) and hyperlipidemia (41.8%, n = 41). Patients were prescribed an average of 4.2 regular medications. Cognitive status was assessed in 19.4% (n = 19) of patients; the Mini-Mental State Examination (MMSE) was used most frequently (89.5%, n = 17), followed by the Clock Drawing Test (CDT) and the Montreal Cognitive Assessment (MoCA) in 5.3% (n = 1) of cases each. In the year of diagnosis, laboratory tests were performed in 88.8% (n = 87) of patients, of whom basic laboratory tests were conducted in 65.3% (n = 64). A total of 25.5% (n = 25) of patients were referred for imaging diagnostics, while 79.6% (n = 78) of patients were referred to clinical specialists: 28.6% (n = 28) to psychiatrists and 51.0% (n = 50) to neurologists. Anti-dementia medication was initiated by family medicine physicians in 9.8% (n = 10) of cases at the time of diagnosis.

***Conclusions:** This study found that there is room for improvement in the diagnosis and treatment of dementia at the primary care level (cognitive assessment, laboratory tests, and imaging diagnostics). In particular, progress is needed in the independent initiation of anti-dementia medications by family medicine physicians.*

INTRODUCTION

Dementia is one of the most pressing public health challenges of modern times. With an aging population, the global burden of this disease is expected to rise steadily. According to the World Health Organization, dementia affects more than 55 million people worldwide, with nearly 10 million new cases diagnosed annually (1). Projections indicate that by 2050, 52 million people will be living with dementia (2). The incidence of disease increases exponentially with age, from 3.1 per 1,000 persons in the 60–64 age group to 175 per 1,000 persons in individuals over 85 years of age (3). Globally, approximately 7.7 million new cases are expected each year—equivalent to one new case every 4.1 seconds (3).

Dementia is a disease characterized by a decline in cognitive function such as memory, thinking, orientation, comprehension, calculation, learning ability, language, and judgment. The degree of decline exceeds what is expected for the individual's age and interferes with daily functioning. The most common forms of dementia include Alzheimer's disease, vascular dementia, dementia with Lewy bodies, and frontotemporal dementia (4). However, not all cognitive impairment is irreversible. Conditions such as vitamin deficiencies, depression, delirium, hypothyroidism, and adverse drug effects may cause

dementia-like symptoms that are treatable.

Family medicine specialists (FMS) are often the first point of contact for patients, and therefore, play crucial roles in the early recognition of dementia and in distinguishing between reversible and irreversible causes. Countries such as the USA, Canada, and Italy have acknowledged the importance of primary care in dementia management and have developed programs based on interdisciplinary collaboration between family physicians and other healthcare professionals (5,6).

A variety of tools are available for the quantitative assessment of cognitive decline, including the Mini-Mental State Examination (MMSE), Clock Drawing Test (CDT), Addenbrooke's Cognitive Examination-Revised (ACE-R), Test Your Memory (TYM), and Montreal Cognitive Assessment (MoCA) (5,7). In Slovenia, two validated and standardized screening tests are used in clinical practice: MMSE and CDT (8,9). At the primary care level, MMSE is used the most (10). It is a short test with a maximum score of 30 points and is a useful screening tool, though relatively insensitive to mild impairment, particularly in highly educated individuals, for whom test modification may be necessary (11). By contrast, CDT is a rapid test requiring approximately 2 minutes to perform, with a reported specificity of 81% and sensitivity of 76% (12,13). Despite the availability of such tools, approximately 65% of dementia cases in primary care remain undiagnosed, delaying timely implementation of care planning and disease management strategies (2,14).

Laboratory testing helps identify reversible or contributing causes of cognitive decline. The basic laboratory test panel includes glucose, electrolytes, calcium, liver and kidney function tests, TSH, and a complete blood count, with additional tests such as vitamin B12, folate, homocysteine, or relevant serologies performed as indicated based on clinical history (7).

In addition to laboratory testing, Slovenian guidelines also recommend neuroimaging, particularly magnetic resonance imaging (MRI) or computed tomography (CT) (7). A non-contrast CT scan of the head is used to exclude structural abnormalities, while MRI provides a more detailed assessment of brain atrophy patterns and is particularly useful in mild or atypical presentations. Advanced imaging methods such as fluorodeoxyglucose-positron emission tomography (FDG-PET) and Single-Photon Emission Computerized Tomography (SPECT) are reserved for specialist evaluation (7). When available, MRI is preferred. Structural imaging is essential for excluding alternative or coexisting conditions such as space-occupying lesions, stroke, normal-pressure hydrocephalus, and other pathologies (15).

The aim of this study was to determine whether patients with newly diagnosed dementia underwent cognitive status assessments, and which assessment tool was used. This study also sought to determine whether patients received laboratory and imaging diagnostics, and whether they were prescribed anti-dementia medication by their family physician or referred to a clinical specialist (neurologist or psychiatrist).

MATERIALS AND METHODS

Study Type

This was a retrospective quantitative descriptive study conducted across six family medicine clinics and one half-time family and occupational, traffic, and sports medicine clinic at the Radovljica Health Center.

Subjects

The study included data from 98 patients treated between January 1, 2014 and November 23, 2018, who had a recorded diagnosis of dementia (ICD-10 codes: F00–F03, F067). Eligible patients were over 75 years of age, had a dementia diagnosis and had a registered personal physician at the Radovljica Health Center. Residents of the Janka Benedik Nursing Home, which is under the jurisdiction of the Radovljica Health Center but managed by a psychiatrist, were excluded. Patients managed by two general practitioners with concessions, those who changed their family physician during the study period, and those treated exclusively in the emergency clinic were also excluded due to a lack of accessible documentation.

Data Collection

Patient data were retrieved from the ISOZ health information system (SRC Infonet d.o.o.) using the previously-mentioned inclusion criteria and recorded ICD-10 codes of F00–F03 and F067 between January 1, 2014 and November 23, 2018. Initial and follow-up visits were included. Data collection focused on diagnostic and therapeutic management at the time of first dementia diagnosis, including whether a cognitive status assessment was performed, the assessment tool used, referrals made, diagnostic tests ordered, and whether anti-dementia medication was prescribed. For all included patients, we also reviewed permanent therapy records in the e-Prescription system, chronic conditions documented in the ISOZ program, and entries in the medical record. Collected variables included gender, age, year of diagnosis, type of cognitive status assessment (MMSE, CDT, MoCA), laboratory testing in the year of diagnosis, referrals for imaging diagnostics, referrals to psychiatry or neurology, comorbid chronic diseases, and chronic therapy.

Statistical Analysis

All data were analyzed using Microsoft Excel 16.0 (Microsoft Office 2016). A descriptive statistical method was used. The study was approved by the Slovenian National Medical Ethics Committee on 17 January 2019 (No. 0120-527/2018/12).

RESULTS

Sample Description

The documentation of 98 patients, 28.6% males (n = 28) and 71.4% females (n = 70), aged 75 to 96 years was reviewed. The exact distribution by age group is presented in Table 1.

Table 1: *Distribution of subjects by age group.*

Age	Number of patients (%)
75-80 years	29 (29.6%)
81-85 years	28 (28.6%)
86-90 years	26 (26.5%)
91+ years	15 (15.3%)

Among associated chronic conditions, arterial hypertension was the most common, affecting 81.6% of patients (n = 80), followed by hyperlipidemia in 41.8% of patients (n = 40), depression in 31.6% of patients (n = 31), heart failure in 28.6% of patients (n = 28), thrombosis and embolism in 26.5% of patients (n = 26), malignancies in 20.4% of patients (n = 20), and diabetes in 20.4% of patients (n = 20). Other notable comorbidities included benign prostatic hyperplasia in 15.3% of patients (n = 15), thyroid disease in 14.3% of patients (n = 14), atrial fibrillation in 14.3% of patients (n = 14), osteoporosis in 12.2% of patients (n = 12), and chronic kidney disease, gastroesophageal reflux, osteoporosis, and atherosclerosis of limb or neck arteries in 6.1% of patients (n = 6).

Cognitive Function Assessment

Cognitive function was formally assessed in 19.4% of patients (n = 19). Family medicine specialists most frequently used the MMSE [used in 17.3% (n = 17) of patients], while the CDT and MoCA were each used in 1.0% (n = 1) of patients. MMSE scores ranged from 7 to 27, with an average score of 20.76. The patient assessed with the MoCA achieved 24/30 points, while the patient assessed with the CDT scored 2/4 points.

Further Diagnostics and Referrals

A total of 79.6% of patients (n = 78) were referred for further management at the secondary or tertiary level. Of those, 28.6% (n = 28) were referred to psychiatry and 51.0% (n = 51) to neurology. The remaining 20.4% (n = 20) were not referred to any specialist. Imaging diagnostics were requested for 25.5% (n = 25) of patients, all of whom underwent head CT scans. No other imaging referrals were documented. In the year of diagnosis, laboratory tests were performed in 88.8% (n = 87) of patients, of whom basic laboratory tests were conducted in 65.3% (n = 64). Detailed results are presented in Table 2.

Prescription of Anti-dementia Medication at the Time of Diagnosis

Of the 98 patients included in the study, anti-dementia medication was initiated by the physician at the time of diagnosis in 9.8% of cases (n = 10). Following

Table 2: *Laboratory tests performed in the year of diagnosis.*

Laboratory tests performed	Number of patients (%)
CBC	87 (88.8%)
Creatinine, urea	78 (79.6%)
Hepatogram (bilirubin, AST, ALT, AP)	67 (68.4%)
Blood glucose	74 (75.5%)
Electrolytes (K)	72 (73.5%)
TSH	56 (57.1%)
B12 and folic acid	34 (34.7%)

referral and further management, additional patients were started on treatment. By 2018, anti-dementia therapy had been introduced in 51.0% of patients (n = 50).

DISCUSSION

Recent global analyses have highlighted trends in mortality related to Alzheimer's disease and other dementias, showing significant variation between countries and regions (16). A study conducted in the Campania region of Italy between 2015 and 2020 reported a steady increase in the incidence and prevalence of all dementias among the elderly population (17).

This study demonstrated that family physicians managing dementia patients often did not fully adhere to existing guidelines, which is consistent with findings from similar international studies (11,15). Dementia diagnoses were most frequently based on subjective reports from patients and family members, while validated cognitive assessment tools were used less often. Only ~20% of patients underwent formal cognitive testing, most commonly with the MMSE, supporting our initial hypothesis. Those results are comparable with data from Canada and Finland (10,18). Similarly, foreign studies show that MMSE is the most frequently used tool (44%), followed by the CDT (12%) and MoCA (7%) (10). A larger systematic study also confirmed that, when time constraints are not a limiting factor, the MMSE remains the most appropriate tool for primary care cognitive assessment (19). In many countries, MMSE testing is mandatory before initiating anti-dementia medication (20). It can therefore be assumed that the limited use of validated tools in our setting, as elsewhere, is largely due to time constraints (10).

Laboratory diagnostics play a central role in dementia assessment, enabling the detection of comorbidities, risk factors, and in some cases, reversible causes of cognitive decline. In this study, we examined laboratory testing at the time of dementia diagnosis to gain insight into diagnostic practices and the frequency of identifying reversible conditions. Testing was performed in most patients. Complete blood counts were most frequently performed, which is in line with guidelines and our expectations. Interestingly, vitamin B12 testing was performed more frequently than in comparable studies, although it remains unclear whether the tests were ordered by family physicians or specialists—a methodological limitation that may affect interpretation of the findings. Findings from a Finnish retrospective study of dementia and mild cognitive impairment patients found that basic blood counts were performed in 89% of patients, electrolytes were measured in 78% of patients, blood glucose in 68% of patients, TSH in 51% of patients, vitamin B12 in 20% of patients, kidney function in 68% of patients, and liver tests in 31% of patients (18). Compared with these data, family physicians in our study ordered basic laboratory investigations (kidney function, liver tests, electrolytes) somewhat less frequently (18).

Imaging diagnostics are an essential component of dementia workup as they help exclude reversible causes of cognitive decline and support more accurate dementia subtype classifications (21). Clinical guidelines, such as those issued by the UK National Institute for Health and Care Excellence (NICE), recommend structural brain imaging, MRI or CT for most patients, except in cases where the diagnosis is already clear (22).

While it may be challenging to determine which patients will benefit most from imaging, studies have shown that routine imaging can improve diagnostic accuracy and treatment planning. Thus, imaging should be considered a standard component of

dementia assessment, as it can significantly influence further clinical decisions (7,14,15). In our study, only about 25% of patients were referred for imaging, all for head CT, with no referrals for MRI. That frequency was lower than expected and below international data. The shortage of family physicians in Slovenia significantly affects the possibility of providing comprehensive patient care, and as a result, patients are often referred to secondary or tertiary levels of care before imaging diagnostics can be performed. Specialists then determine whether imaging diagnostics are necessary. Additionally, access to imaging is significantly faster when the examination is performed during hospitalization. International guidelines and the Slovenian recommendations state that imaging diagnostics should be used to exclude secondary causes (e.g., tumor, hematoma, hydrocephalus) in atypical cases (4,22).

More than half of the patients in this study were referred to clinical specialists, most often neurologists and less frequently psychiatrists. This referral rate was higher than in comparable studies abroad, which may reflect the heavy workload of family physicians in Slovenia as well as the fact that they were only authorized to prescribe anti-dementia medication beginning in 2018. Prior to 2018, the guidelines required a referral upon suspicion of cognitive decline. Since 2018, family physicians have gained the competence to initiate therapy independently; however, in our study, anti-dementia treatment was started at the primary care level in fewer than 10% of patients.

The main limitations of this study were the relatively small sample size (98 patients) and its single-center design, which limit the generalizability of the results. A limitation of our study was also the use of only descriptive statistical methods. Due to the patient selection method, individuals with undocumented dementia diagnoses may have been excluded. We also identified gaps in documentation that may have reduced data accuracy. In several cases, it was unclear whether laboratory tests were ordered directly by family physicians or by specialists. For patients diagnosed early in the calendar year, some test results from the previous year may have been included, potentially underestimating the actual frequency of testing. Similar limitations apply to cognitive testing and referrals. As data were obtained solely from medical records, it is possible that some tests or referrals were performed but not documented. Finally, the study period (2014–2018) largely predated the time when family physicians in Slovenia gained the authority to prescribe anti-dementia medications, which may have influenced the prescribing patterns. This study paves the way for future research, which should be conducted on larger, multicentre cohorts with prospective data collection.

CONCLUSIONS

Our findings highlight several challenges in dementia care at the primary level, including limited consultation time, administrative burden, lack of specialized knowledge, and incomplete documentation of procedures. To improve care quality, additional training for family medicine specialists and enhanced coordination between primary, secondary, and tertiary care are required. For better diagnostics and early disease detection, public education would play an important role and also, the establishment of dementia centers, where care would be more targeted and diagnostic procedures more accessible. Prior to referral to such a center, it would be recommended that the patient completes the MMSE test at the family physician's office.

Despite the limitations to this study, it provides a valuable foundation for future research and emphasizes the need for improving the quality of care for dementia patients in family medicine.

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Z natančnim načrtovanjem implantacije lahko vplivamo na potrebo po srčnem spodbujevalniku po TAVI, to pa lahko predvidimo z vrednostjo troponina po posegu

The Need for a Pacemaker after TAVI can be Influenced by Careful Planning and Predicted by Higher Troponin Values after Implantation Study

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Izvleček

Namen: *Transkatetrsko implantacijo aortne zaklopke (TAVI) spremljajo prevodne motnje, ki lahko zahtevajo vstavitev trajnega srčnega spodbujevalnika (PM). Obstajajo nekatere specifične značilnosti, ki so povezane z večjo potrebo po implantaciji srčnega spodbujevalnika. Te so odvisne od bolnika in povezane s postopkom implantacije.*

Metode: *Analizirali smo retrospektivne podatke za en sam center, kar vključuje 150 bolnikov s TAVI v letu 2023, od katerih je 14 bolnikov še imelo vstavljen PM. Dva sta bila izključena zaradi operacije in ponovne TAVI v istem mesecu.*

Rezultati: *Na podlagi CT (angl. Computer Tomography) analize so operaterji izbirali med dvema vrstama transkatetrskih srčnih zaklopk*

Abstract

Aim: *Conduction abnormalities that require the implantation of a permanent pacemaker (PM) are known to accompany transcatheter aortic valve implantation (TAVI). Specific patient-dependent and procedure-related features are known to correlate with higher pacemaker implantation rates.*

Methods: *We analysed retrospective data from a single centre with 150 TAVI cases in 2023. Fourteen cases had a PM already implanted and two were excluded due to a change to surgery and repeated TAVI in the same month.*

Results: *Two types of transcatheter heart valves (THVs) were implanted and chosen based on computer tomography scans. Nineteen patients (14%) required PM after TAVI*

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(THV). 19 bolnikov (14 %) je po TAVI potrebovalo PM in vsi so bili vstavljeni v isti hospitalizaciji. Vrsta vstavljene THV ni bila povezana s potrebo po PM. Bolniki, ki so potrebovali PM, so pogosteje imeli predhodnji desnokračni blok (20 % v primerjavi z 9 %, p = 0,355), vendar ta ni bil statistično značilen. Imeli so višje vrednosti troponina (p = 0,012) in potrebovali daljšo hospitalizacijo (p = 0,007). Na prvem ambulantnem pregledu so imeli tisti z vstavljenim PM v povprečju 95 % ventrikularnega stimuliranja, ni prišlo do upada iztisnega deleža levega prekata in ni bilo razlike v trimesečnem preživetju v primerjavi z bolniki brez vstavljenega PM.

Zaključki: *Potrebo po PM po TAVI je mogoče predvideti in se ji do neke mere izogniti. Vsak postopek TAVI je treba skrbno načrtovati. Ustrezno vstavljen PM ne predstavlja tveganja za kratkoročno preživetje.*

and all underwent implantation in the same hospital. There was no difference in the type of THV implanted. Patients that required PM had preexisting right bundle branch block more frequently (20% vs. 9%, p = 0.355), but this was not significantly different. They had however, have significantly higher values of troponin (p = 0.012) and required longer hospitalisations (p = 0.007). On first outpatient control, patients with PM implants had an average of 95% of ventricular pacing, no difference in ejection fraction, and no difference in three month survival compared to patients without a PM implanted.

Conclusions: *The need for a PM after TAVI can be predicted and avoided to some point. Every TAVI procedure should be carefully planned. Well implanted PMs carry no risks for short term survival.*

INTRODUCTION

Transcatheter aortic valve implantation (TAVI) is an established therapeutic method for the treatment of aortic stenosis (1). Due to transcatheter heart valve (THV) interactions with tissue under the aortic anulus and in the left ventricular outflow tract (LVOT), it is possible to damage conduction tissue in the bundle of His and bundle branches, thus, causing infranodal aortic valve (AV) block. Left bundle is especially vulnerable to infranodal AV block as it lies just beneath the membranous septum and is relatively shallow in the myocardium. Some anatomical features (2), preexisting diseases, and TAVI technology (3) (4) are linked to higher rates of conduction abnormalities after TAVI. THV design and implantation depth was also shown to influence conduction abnormalities (CAs) (5). Due to stent frame compression and oedema, THV can cause AV block or left bundle branch block (LBBB). LBBB is often self-resolving and patients can be dismissed without PM (6). Although new LBBB occurs frequently, it is not linked to progression to AVB and the need for early PM implantation (7). The latest guidelines recommend PM implantation in persistent AVB with the same recommendations as in the non-TAVI population (8). The only difference is the time interval from detection to implantation. Some studies implied that PM implantation is linked to worse outcomes after TAVI (9), making need for PM a complication. Time is crucial to lower the PM rate and avoid PM implantations that do not need pacing on further follow up (10).

The aim of this retrospective study was to compare data on implantation rates, potential preexisting factors, and implantation outcomes relative to the existing literature.

MATERIALS AND METHODS

This retrospective study analysed 134 consecutive patients without previously implanted PMs that underwent TAVI in the University Medical Centre Maribor in 2023. Patients with PM implanted more than one month after TAVI were deemed to be not TAVI related. All data were collected form patient reports form TAVI centre or hub hospitals, and no

additional tests were performed out of daily clinical practice for the purpose of this observational study. All patients underwent pre- and post-procedural 12-lead ECG, pre- or post-dilatation, and implanted THV. There were two types of THV used, including balloon expandable (BEV) Sapien 3 by Edwards, and the self-expandable (SEV) Navitor by Abbott. We recorded indications for PM implantation on the day of PM implantation after TAVI. All implant patients had scheduled outpatient visits with PM assessments to collect data on the percentage of ventricular pacing. Three-month survival was recorded by TAVI outpatient clinics. We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research.

CONDUCTION ABNORMALITY

Bundle branch block (BBB) was defined as a QRS > 120 ms and further defined as right bundle branch block (RBBB) or LBBB according to QRS morphology. High degree AVB was considered first degree AVB with a PQ > 280 ms, second degree AVB Mobitz II when awake, and complete AV block or bradycardic atrial fibrillation (AF) with pauses longer than 6 s.

TAVI

Preprocedural computer tomography (CT) scans were carefully examined for the degree of aortic valve leaflet calcination, LVOT morphology, and calcination and aortic root. Two types of THV were implanted: SEV Abbot Navitor and BEV Edwards Sapien 3. The operators chose the THV type based on CT measurements, but the exact reason was not written in majority of case reports. Annuli sized 430 mm2 are most often considered as small annuli. We did not have systematic measurements of annulus size or the extent of valve calcification before TAVI. However, because the Sapien 3 23 mm and Navitor 25 mm can accommodate a maximal area of 430 mm2, we used those sizes as cut-offs. Predilation was performed in cases of heavily calcified valves, based on the operators' preferences. A pre-dilation balloon was used based on the minimum anulus diameter. In cases of frame compression after implantation, THV was post-dilated with a balloon chosen according to the average anulus diameter.

PM IMPLANTATION AND FOLLOW-UP

PM was implanted in cases of complete AVB lasting longer than 24 hours. In cases of first degree AVB with a PQ > 280 ms, second degree AVB Mobitz II, or pauses longer than 6 s in AF when awake, patients were observed closely. The number of days from TAVI to PM implantation were recorded. PM follow-up was performed on average two months after implantation.

LABORATORY TESTS

We recorded serum troponin I with a Siemens Dimension Vista system 12–24 h after TAVI. Serum troponin I is measured routinely after all invasive procedures to determine mortality risk. Other laboratory parameters and baseline troponin values were not collected.

STATISTICAL ANALYSIS

Jamovi 2.5 was used for statistical analysis. The Mann–Whitney U test and χ^2 test were used for contingent tables. P-values < 0.05 were considered statistically significant.

RESULTS

We collected data from TAVI patients at the University Medical Centre Maribor in 2023. One-hundred fifty patients were screened, and 14 were excluded because they had a PM already implanted before procedure. One patient was later excluded due to acute complication that resulted in THV explant and surgical aortic valve replacement. A second patient was excluded due to repeated TAVI due to a severe paravalvular leak. Retrospective data for 134 consecutive patients were used for statistical analysis.

Nineteen patients (14%) required PM implantation after TAVI.

The study population was elderly with an average age of 80 years. Female patients were represented at 41% and they required a PM at a frequency of 19% compared to 13% in males. Age, height, and weight did not predispose the group to PM (Figure 1). Preexisting RBBB was observed in 13 patients (10%) and did not predispose to PM implantation after TAVI (p = 0.355). BEV was implanted more frequently (Sapien 3, in 66%) than SEV, but PM was implanted with similar frequencies, irrespective of the THV type used (p = 0.187). Coronary disease with previously implanted stent, status of post-surgical revascularisation, or known chronic total occlusion of coronary artery (CTO) were present in 25% of cases. Flow limiting stenosis was used during TAVI in three cases. Thirty-one patients (23%) had a small anulus assumed by the size of the valve implanted (Sapien 3 size 23 mm, Navitor 25 mm or smaller). A small anulus size and coronary artery disease did not predispose for PM (p = 0.335 and p = 0.215). Accessible demographic data are represented in Table 1.

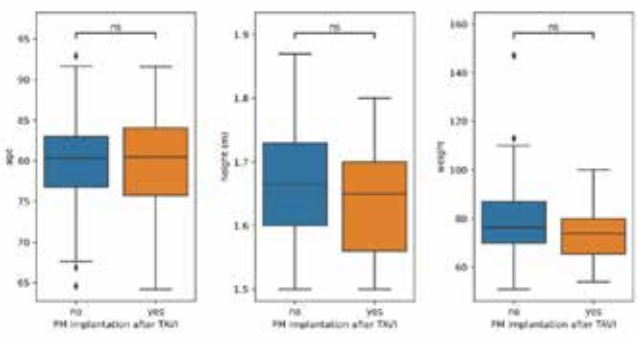

Figure 1. *Age, height, and weight - PM vs. no PM*
Age, height, and weight - PM vs. no PM. There was a slight trend towards smaller and shorter patients in the group with fewer PM patients.
PM, pacemaker; TAVI, transcatheter aortic valve implantation; ns, not significant

Nineteen out of 134 patients had PM implants due to symptomatic high-degree AVB (14%). On average, PM was implanted on day 5 after TAVI (Figure 2). Patients that had PM implants more than one month

Table 1: *Demographics*

		Total	No PM implantated post TAVI	PM implantated post TAVI	p-value
All		134	115 (85.8%)	19 (14.2%)	
Weight (average kg)		78	79	73	0.217
Height (average cm)		167	163	166	0.211
BMI (average)		28	28	27	0.754
Sex	Male	78	68	10	0.574
	Female	56	47	9	
CAD	Yes	34	27	7	0.215
	No	100	88	12	
RBBB	Yes	13	10	3	0.355
	No	121	105	16	
Small annulus	Yes	31	25	6	0.335
	No	103	90	13	
SEV	Yes	46	37	9	0.187
	No	88	78	10	

Demographic data of patients undergoing TAVI in 2023 did not predict the need for PM.
BMI, body mass index; CAD, coronary artery disease; RBBB, right bundle branch block; SEV, self expandable valve; PM, pacemaker; TAVI, transcatheter aortic valve implantation

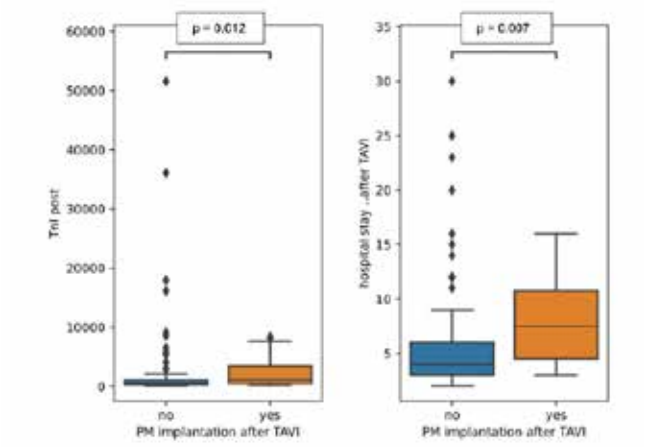

Figure 2. *Troponin I and hospitalisation - PM vs. no PM TnI and hospitalisation - PM vs. no PM. Patients that required PM implantation after TAVI had higher TnI levels and required prolonged hospital stays.*
PM, pacemaker; TAVI, transcatheter aortic valve implantation; TnI, troponin I

after TVI were considered as not being TAVI related. Periprocedural and in-hospital data were available for all 134 patients. Eleven patients were transferred to local hub hospitals one day after procedure and we did not include their length of hospital stay due to different local policies. The length of hospital stay in Maribor was significantly longer in cases where patients required a PM (p = 0.007), lasting 6 days on average. On average, TAVI patient were discharged after 5 days (Figure 2).

A significantly higher level of troponin I (TnI) was observed after TAVI in patients that required PM implantation (p = 0.012). Three months survival data were available for 128 patients. PM implantation did not affect survival rate (p = 0.678).
Despite low numbers, pre-dilatation or post-dilatation did not predispose patients to for PM implantation (Table 2).

DISCUSSION

The need for PM after TAVI varies among studies and has changed with the technical advancements of THVs. The need for PM after TAVI was traditionally considered as a failure of TAVI based on comparisons to surgical aortic valve replacement. The latest guidelines on pacing (8) with special consideration of pacing after TAVI suggest that PM is needed in 3.4% to 25.9% of cases. Some patient characteristics, THV design, and implantation depth are linked to higher PM implantation rates. Therefore, to achieve lower PM rates, we must understand patient characteristics during planning and adjust the implantation strategy to achieve optimal TAVI results.
Our one-year registry data represent real-life situations in clinical practice. Since the number of implanted PMs also depends on the type of THV used, our data are representative of approximately 50% BEV and 50% SEV implants. The data are from a retrospective registry, and one should consider the significant bias as THV was chosen based on patient characteristics.

Table 2: *Pre- and post-dilatation*

Total			No PM implantated post TAVI	PM implantated post TAVI	p-value
Predialtation	Yes	38	30	8	0.144
	No	96	85	11	
Postdilatation	Yes	8	6	2	0.360
	No	127	110	17	

Pre- and post-dilatation. Patients that had pre-dilatation or post-dilatation during TAVI implantation did not have higher PM implantation rates.
PM, pacemaker; TAVI, transcatheter aortic valve implantation

To date male sex, RBBB (11), calcinations in LVOT at the level of the non-coronary cusp (12), and membranous septum morphology (2) are predictors of a higher need for PM implantation. One of the strongest predictors of PM implantation after TAVI is preexisting RBBB (3). Interestingly, we did not observe the same correlation in our registry. Thirteen patients (10%) had a preexisting RBBB, but only three required PM after TAVI. Therefore, RBBB did not predispose to PM implantation after TAVI in our group. Most patients with preexisting RBBB had a BEV implanted (in 85% of cases) and the valve type was selected by the operators. BEVs are known to cause less CA compared to SEV (13). Thus, operators may have chosen BEV in RBBB patients, which resulted in a lower number of PM implantation in this specific population.

Our study patients had an average age of 80 years and were reffered for TAVI based on the 2021 guidelines on age, surgical risk score, and comorbidities. They were predominantly males (58%), but sex did not predict the need for PM after TAVI.

Aortic valve calcifications are linked to CA abnormalities after TAVI (6) and several studies have stressed the importance of calcium volume and distribution on aortic valves, annulus, and LVOT (14). A short length of membranous septum is also linked to higher PM implantation rates. (2) Those measurements demand special imaging protocols that are not routinely used in our environment, and therefore, we routinely assess the degree of calcification only visually during pre-TAVI planning. Thus, we were unable to gather numerical data on the amount of calcium in valves in the study population.

Pre-dilatation is linked to higher PM implantation rates. It is used to open the native valve to allow easier crossing and deployment of THV. Therefore, pre-dilatation is a marker of a high degree of aortic valve calcination. The more calcified the valve, the more often is it predilated, and the higher the chances of conduction abnormalities that require PM implantation in case of SEV implants (15). In our study, predilation was performed at the operator's discretion in 38 cases, but was not correlated with the need for PM ($p = 0.144$). Pre-dilatation was performed less frequently in cases of BEV implantation compared to SEV (BEV 14% vs. in SEV 48%). Nevertheless, the SEV used in our centre is known for its lower radial force, and we tend not to use it in heavily calcified valves, which may have influenced our results.

Due to the THV design and the nature of implantation, THV itself can cause infranodal AV block due to His bundle compression or LBBB in cases of isolated left bundle compression. The occurrence rate depends on the THV design; the bigger the stent frame, the more tissue it interferes with and more it compresses delicate structures. SEV platforms with large stent frames extend low in the LVOT and are more prone to causing conduction abnormalities than BEV platforms (16). Therefore, we suggest to implant SEVs high in the native anulus to reduce the contact of the stent frame with LVOT tissue. Our data showed no differences between the THV type implanted in patients with conduction disturbances requiring PM, and thus, we can conclude that we implanted our THVs high.

Comparing literature to time, indication for PM implantation varies. In the current study, we adhered to current guidelines on PM implantation (8). In most patients with first degree AV block and LBBB, conduction abnormalities disappeared during prolonged observation and they did not meet the indications for PM implantation (17). All patients were examined two months after PM. After implantation, pacing frequency was set to 50 beats per minute (bpm) or lower. PM patients had an average of 78% of ventricular pacing, only two had no or 1% pacing, and one had 14% pacing two months after PM implantation.

In our practice, we do not routinely record the frequency of escape or intrinsic rhythm during back-up pacing at 30 bpm on follow-up examination. Majority of patients had high percentage of ventricular pacing. However, three patients with low pacing rates had low values of < 10% and we conclude those patients may be overtreated.

Elevated troponin levels after invasive procedures is linked to a higher risk for adverse events (18). The same is true for elevated preprocedural levels of high sensitivity troponin before TAVI (19). Koifman et al. found that patients with elevated troponin levels after TAVI have more frequent CA (20). We

also made similar findings in this study. Elevated troponin can be explained by direct tissue damage during implantation, because of hypoperfusion durnig rapid pacing for THV deployment or due to possible calcium embolisation and direct ischemia. because of hypoperfusion during rapid pacing or slow THV deployment, and direct ischemia due to calcium embolization.

The sample size in this study was too small for subgroup analyses of different THV types, preexisting heart failure, or concomitant coronary artery disease. Much larger studies managed to prove that troponin is a good marker for mortality and adverse events, but its levels are influenced by many factors, and therefore, inappropriate to make conclusions.

During a 1 year follow-up of 19 patients with PM implanted after TAVI, none were hospitalised for heart failure. However, we did not observed a worsening of ejection fraction on control echocardiography compared to patients who did not need PM. However, data on ejection fraction before and after PM implantation were only available for PM patients. Data on QRS duration after PM implantation were not available, but based on implantation reports, all ventricular leads were implanted in the septal position. That could also be the reason for less pacemaker induced cardiomyopathy and heart failure. Since there is a strong trend of physiological pacing worldwide, we still miss data on septal pacing or LBBB pacing after TAVI.

Predicting CA after TAVI is challenging. Some centres prefer early or prophylactic PM implantation to facilitate mobilisation and discharge. Every device implanted without a benefit is a risk for the patient. Consequently, the latest guidelines on pacing recommend prolonged observation (8). In our experience, complete recovery is possible, even in some cases with complete AV block immediately after TAVI. Prolonged observation resulted in significantly longer hospitalisations in patients with CA. In our cohort, patients were observed for an average of 5 days before implanting a PM. Therefore, we suggest additional tests and decision models that predict irreversible CA within a short observation time.

We revealed that maximum adaptation of an implantation strategy and THV selection based on patient characteristics can lower the PM rate, however, high levels of troponin can predict PM implantation and may shorten hospitalization duration due to earlier PM implantation without the fear of overtreatment. The main limitation of this study is the relatively small number of pacemaker implantations after TAVI as the main event. Our data were observatory and it lacks long term follow up. The use of two different THV types rendered the results complex, and this should be taken into account when analysing real word data.

CONCLUSION

The need for PM after TAVI is relatively common. This retrospective study showed that the consideration of factors such as preexisting RBBB when contemplating THV selection and high THV implantation can lower the PM implantation rate. More data are needed for additional parameters, such as troponin elevation after TAVI, to facilitate a final decision on PM implantation and shorten the time from TAVI to discharge. In patients that require PM after TAVI, a properly implanted device had a high percentage of ventricular pacing and low rate of PM cardiomyopathy.

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Učinek ortopedsko-ortodontske obravnave nepravilnosti razreda II, oddelek 1

Treatment effects of dentofacial orthopedics followed by a multibracket appliance for Class II division 1 malocclusion

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Ključne besede:
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Izvleček

Namen: *Namen te študije je bil ovrednotiti učinke dvofaznega ortodontskega zdravljenja nepravilnosti razreda II, podrazred 1, ter tudi jih primerjati z normalno rastjo pri nezdravljenih primerih razreda II (kontrolna skupina).*

Metode: *V študijo je bilo vključenih 27 pacientov (17 fantov in deset deklet). Analiza je temeljila na stranskih telerentgenih, opravljenih pred začetkom zdravljenja (T0), po zdravljenju s funkcionalnim ortodontskim aparatom v pubertetnem obdobju (T1) ter po zaključenem zdravljenju s fiksnim ortodontskim aparatom za dosego optimalne okluzije (T3). Povprečna starost pacientov pred začetkom zdravljenja s funkcionalnim aparatom je bila 11,7 ± 0,7 let (CVMS 2–4). Učinke rasti smo*

Abstract

Purpose: *The aim of this study was to evaluate the effects of a two-phase orthodontic treatment for Class II division 1 malocclusion and to compare the outcomes with the natural growth observed in untreated Class II subjects.*

Methods: *The study group consisted of 27 patients (17 males and 10 females). Lateral cephalograms were evaluated before treatment (T0), after treatment with a functional orthodontic appliance during puberty (T1), and after treatment with a fixed appliance to achieve proper occlusion (T3). The mean age of patients before functional appliance therapy was 11.7 years (±0.7; Cervical Vertebral Maturation Stage (CVMS) 2–4). The effect of growth was assessed by compar-*

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primerjali z nezdravljeno kontrolno skupino pacientov z nepravilnostjo razreda II.

Rezultati: *V primerjavi z nezdravljeno skupino je prva faza zdravljenja s funkcionalnimi aparati povzročila statistično pomembno povečanje efektivne dolžine mandibule, zmanjšanje skeletnega sagitalnega neskladja med maksilo in mandibulo, izboljšanje obraznega profila ter zmanjšanje sagitalne stopnice (SS). To zmanjšanje je bilo posledica protruzije in proklinacije zgornjih sekalcev ter retruzije in retroklinacije spodnjih sekalcev (p ≤ 0,022). Čeljustna ortopedija ni imela statistično pomembnega vpliva na vertikalno dimenzijo obraza. Druga faza zdravljenja s fiksnim aparatom je v primerjavi s kontrolno skupino prispevala k zmanjšanju vertikalne dimenzije obraza ter dodatnemu zmanjšanju SS, in to predvsem zaradi protruzije in proklinacije spodnjih sekalcev (p ≤ 0,046).*

Zaključek: *Prva faza zdravljenja nepravilnosti razreda RII/1 je imela izrazitejše učinke kot druga faza zdravljenja. Kljub temu sta obe fazi zdravljenja pokazali večji dentoalveolarni kot skeletni učinek.*

ing the results to untreated Class II cases in the control group.

Results: *Compared to untreated individuals, first-phase treatment with functional appliances significantly increased the effective mandibular length, reduced maxillo-mandibular sagittal skeletal discrepancy, improved the facial profile, and decreased overjet through the protrusion and proclination of maxillary incisors and the retrusion and retroclination of mandibular incisors (p ≤ 0.022). Dentofacial orthopedics did not significantly affect the vertical facial dimension. In the second phase, treatment with fixed appliances reduced the vertical facial dimension and reduced overjet, primarily through proclination and protrusion of the mandibular incisors (p ≤ 0.046).*

Conclusions: *The first phase of Class II division 1 treatment produced greater effects than the second phase. In both phases, changes were predominantly dentoalveolar rather than skeletal.*

INTRODUCTION

Class II malocclusion is typically defined by an anteroposterior discrepancy between the dental arches. The condition becomes more pronounced when it is associated with skeletal imbalance resulting from mandibular retrognathia, maxillary prognathia, or a combination of both (1,2). Skeletal Class II malocclusion is a frequently encountered clinical problem in orthodontics. Data from the National Health and Nutrition Examination Survey III indicated a prevalence of Skeletal Class II malocclusion of approximately 23% in children, 15% in adolescents, and 13% in adults (2). In most individuals, this malocclusion is primarily related to mandibular retrognathia (1,3).

The etiology of Class II malocclusion is multifactorial; therefore, treatment planning must consider several factors, including the patient's stage of skeletal development, the optimal timing of intervention, the severity of the malocclusion, and the choice of orthodontic appliance (4). In growing patients presenting with mandibular retrognathia, functional appliances are widely used to correct Class II malocclusion (2,5,6). Functional appliances, whether removable or fixed, are designed to reposition the mandible sagittally and vertically, thereby promoting orthodontic and orthopedic adaptations in the jaws and dentition (7–10). Commonly used removable functional appliances include the Twin Block appliance (7,10–13), the Sander bite-jumping appliance (14–16), and the mandibular advancement appliance used with Invisalign (17). Fixed functional appliances frequently used in clinical practice include the Herbst appliance (18,19), Forsus (20), Jasper Jumper (21–23), and the mandibular anterior repositioning appliance (24).

The dentoskeletal effects produced by functional appliances may vary depending on the timing of treatment. When therapy is initiated during the pubertal growth spurt, or shortly thereafter, skeletal

changes such as increased mandibular length may occur (25,26). Treatment may also contribute to the correction of molar relationships, alignment of incisors, improvement of overjet (OJ) and overbite, and the modification of skeletal relationships (5). However, removable functional appliances are often perceived by patients as uncomfortable and unaesthetic, and the success of treatment largely depends on patient compliance and motivation (27). Nevertheless, some investigators have suggested that the observed treatment effects are predominantly dentoalveolar (8,13) and may be comparable to those achieved through normal growth or conventional edgewise therapy (28,29).

Treatment of Class II malocclusion associated with mandibular retrognathia in growing patients remains challenging. Moreover, some improvements achieved during the first phase of treatment, particularly OJ reduction, may be partially lost during the second phase due to dental decompensation during leveling and alignment, or an unrecognized pterygoid response. Therefore, the aim of this study was to evaluate the impact of treatment with a functional appliance followed by fixed appliance therapy on dentoskeletal characteristics. The primary outcome was dental change, specifically OJ, while secondary outcomes included skeletal changes and changes in the soft tissue facial profile.

The null hypothesis was that treatment mainly produces dentoalveolar changes, but more skeletal changes in the functional appliances phase than the fixed appliance phase. It was anticipated that the increase of mandibular length and the decrease in facial convexity was greater in treated patients than untreated controls.

MATERIALS AND METHODS

Data acquisition

This study protocol was reviewed and approved by the University of Rijeka Ethics Committee (No. 2170-24-01-15-2) and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from the parents of all participants prior to inclusion in the study.

Groups

The data were collected from a previously-described one-center study on functional appliances (30).

The patients were considered eligible for the first phase of treatment if they presented a full Class II division 1 malocclusion associated with mandibular retrognathia, an OJ ≥ 5 mm, skeletal maturity corresponding to cervical vertebral maturation stage CVMS 2-4 (26,31), absence of chronic diseases or medical conditions, and Croatian as their native language. The exclusion criteria included vertical facial growth patterns and mental disability.

Twenty-seven patients had complete records available after undergoing treatment with a labial multibracket full fixed straight-wire appliance (McLaughlin, Bennett, and Trevisi (MBT) prescription, 0.022"), without premolar extractions, which was used to finalize and detail the occlusion. Both dental arches were leveled and aligned up to a 0.019" × 0.025" stainless steel archwire, and Class II elastics were applied. The control group consisted of Caucasian individuals selected from the Bolton-Brush, Oregon, Forsyth, and Michigan growth studies (American Association of Orthodontists Craniofacial Growth Legacy Collection). Controls were matched to the treated patients according to skeletal class, sex, and skeletal age.

Lateral cephalograms

Lateral cephalograms (LCs) in the study group were obtained before treatment (T0), at the completion of functional appliance therapy (T1), and immediately before removal of the full fixed appliance (T2). Cephalograms from the untreated control group were collected at the corresponding time intervals.

All LCs were obtained using a standardized cephalometric technique with a cephalostat and a calibration ruler. Only high-quality images without exposure or positioning errors were included in the analysis.

Craniofacial morphological characteristics were analyzed by a single examiner (AF), an orthodontist, using the Audax cephalometric software program (Audax, Ljubljana, Slovenia). The list of cephalometric variables is presented in Table 1.

To assess intra-examiner reliability, measurements

of 27 LCs were repeated after a 1-week interval. Reproducibility was evaluated using the intraclass correlation coefficient.

Statistical analysis

The Mann–Whitney U test was used to compare changes in cephalometric variables (T0 – T1 and TI – T2) between the study and control groups. A p-value of 0.05 was considered statistically significant.

RESULTS

Figure 1 indicates the patient progression throughout the clinical trial. Patients whose treatment included tooth extractions were excluded from the study, as extractions may compensate or alter the facial and skeletal profile.

The mean age of patients at the beginning of treatment with a functional appliance was 11.7 years (±0.7 years). The functional appliance phase lasted ~1 year.

Twenty-seven patients treated with a functional appliance subsequently underwent treatment with a full fixed labial multibracket appliance (straight-wire appliance) to finish and detail the occlusion.

The mean (± standard deviation) duration of treatment with the fixed appliance was 27.3 months (±9.01 months). The sex distribution in the treated group consisted of 17 males and 10 females, which was identical to that of the control group. No statistically significant differences were observed between the groups with respect to initial age at treatment or sex distribution ($p > 0.05$).

Treatment effects of functional appliance

Differences in cephalometric measurements before (T0) and after (T1) treatment with a functional appliance are reported in Table 2.

Compared to untreated subjects, the functional appliance group showed a significant increase in the Sella-Nasion-B point (SNB) angle and total mandibular length, as well as a significant decrease

Table 1. Linear and angular measurements and descriptions.

Measurement	Definition
SNA (°)	Prognathism of the maxillary alveolar bone, angle formed between the SN plane and point A
SNB (°)	Prognathism of mandibular alveolar bone, angle formed between the SN plane and point B
ANB (°)	Skeletal sagittal class angle, difference between SNA and SNB angle relates jaws to anterior cranial base
Wits (mm)	Skeletal sagittal class appraisal, linear distance between the projecting points A and B perpendicular on the functional occlusal plane (AO and BO). Positive value when AO precedes BO
NAPg (°)	Skeletal facial convexity, angle formed between the N-A line and A-Pg line
AnsPns/ MeGo (°)	Intermaxillary angle, angle between palatal and mandibular plane
SGo/NMe	Face height ratio, the ratio between posterior face height (S-Go) and anterior face height (N-Me)
SNGn (°)	Facial skeltal Y axis, angle between N-S-Gn
Björk polygon (°)	Sum of angles N-S-Ar, S-Ar-Go, Ar-Go-Me
Co-Gn (mm)	Total mandibular length, the linear distance between the condylion and the gnathion points
U1/AnsPns (°)	Maxillary incisor inclination, the angle between the most prominent maxillary incisor (Is-As) and the palatal plane
L1/GoGn (°)	Mandibular incisor inclination, the angle between the most prominent mandibular incisor (Ii-Ai) and the mandible plane
U1/NA (°)	The angle between the long axis of the upper incisors to the NA plane
L1/NB (°)	The angle between the long axis of the lower incisors to the NB plane
OJ (mm)	The horizontal distance from the maxillary incisor tip to the labial surface of the mandibular incisor
Gl-Sn-Pg'	Facial convexity, the angle between soft tissue Gl, Sn, Pg'

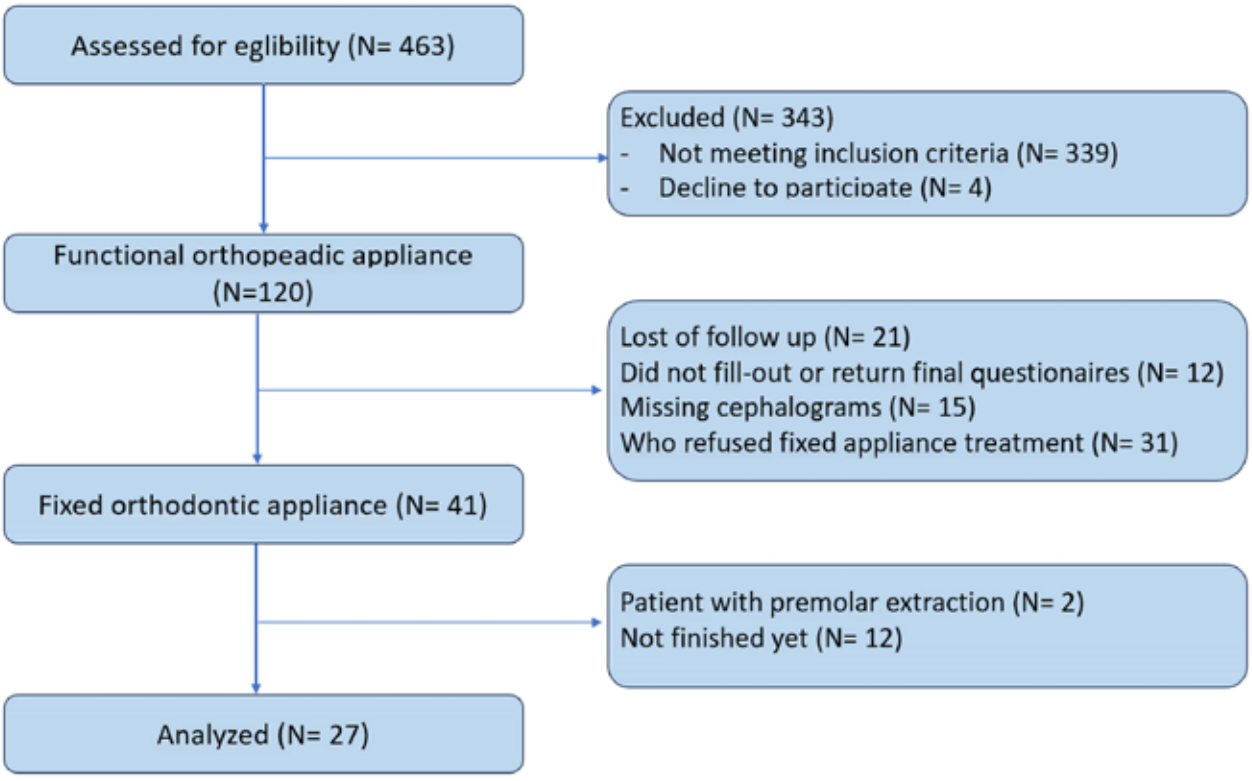

Figure 1. *Diagram of patient progression.*

in the A point-Nasion-B point (ANB) angle and Wits appraisal, while no significant differences were observed in vertical measurements. The inclination and protrusion of the maxillary incisors significantly decreased, whereas the inclination and protrusion of the mandibular incisors increased compared to the untreated group.

Treatment with a functional appliance improved the facial profile with a reduction in facial convexity due to an increase in the Nasion-A point-Pogonion (NAPg') and Glabella-Subnasale-Pogonion (Gl-Sn-Pg') angles.

Treatment effects with fixed orthodontic appliance

Differences in cephalometric measurements after (T2) treatment with the fixed orthodontic appliance and at the end of treatment with the functional appliance (T1) are reported in Table 3. An increase in the Wits measurements and a decrease in the vertical dimension (Björk) was observed following treatment with a fixed orthodontic appliance. The reduction in OJ observed in the treated group compared to the untreated group was also observed with an increase in mandibular incisor inclination and protrusion. A greater protrusion of the maxillary incisors was also observed in the treated group compared to the control group.

DISCUSSION

The present study demonstrated that a greater treatment effect in Class II division 1 malocclusion was achieved during the first phase with a functional appliance than during the second phase with a fixed multibracket appliance combined with Class II elastics. The majority of the treatment effect observed in both phases was dentoalveolar, and therefore, the null hypothesis was partially accepted.

Effects of functional appliance therapy

Treatment with a functional appliance during active growth resulted in statistically and clinically significant skeletal changes compared to untreated

Table 2. Treatment effects with functional appliances (T1–T0) compared to the control group.

Variable	Treated group median (interquartile range)	Control group median (interquartile range)	p
SNA (°)	0.2 (-0.1-0.7)	-0.4 (-1-0.9)	0.130
SNB (°)	1.4 (0.6-2.0)	0.2 (-0.4-1.0)	≤ 0.001
ANB (°)	-0.8 (-1.8-(-0.5))	-0.5 (-0.8-0.4)	0.003
Wits (mm)	-2.0 (-3.0-(-2.0))	-0.1 (-1.0-1.2)	≤ 0.001
NSGn (°)	-1 (-1-3)	0 (-0.7-0.7)	0.411
NAPg (°)	-2.4 (-4.7-(-1.2))	-0.9 (-2.5-1.3)	0.003
AnsPns/MeGo (°)	-0.5 (-1.4-0.7)	-0.7 (-2.3-1.6)	0.782
SGo/NMe (%)	0.9 (-1.4-2.6)	0.0 (0.0-0.0)	0.622
Björk's sum (°)	-1.0 (-2.2-0.8)	0.2 (-1.2-1.0)	0.183
Co-Gn (mm)	7.0 (5.0-9.0)	2.8 (1.0-3.6)	≤ 0.001
U1/AnsPns (°)	-4.7 (-7.5-(-2.0))	0.0 (-2.3-2.0)	≤ 0.001
L1/GoMe (°)	2.6 (0.7-5.0)	0.5 (-1.0-1.7)	0.005
U1/NA (mm)	-1.5 (-2.6-(-0.8))	0.2 (-0.5-1.0)	≤ 0.001
L1/NB (mm)	1.8 (0.0-2.6)	0.2 (-0.1-0.4)	0.022
OJ (mm)	-3.9 (-5-(-2.5)	0 (-1-0.7)	≤ 0.001
Gl-Sn-Pg' (°)	2.2 (1.3-3.9)	(-1.4-3.0)	0.022

Table 3. Treatment effects with fixed orthodontic appliance (T2-T1) compared to the control group

Variable	Treated group median (interquartile range)	Control group median (interquartile range)	p
SNA (°)	0.0 (-0.1-0.9)	0.3 (-0.7-1.4)	0.169
SNB (°)	0.4 (-0.2-1.5)	1.6 (0.1-3.1)	0.067
ANB (°)	-1.0 (-1.8-0.0)	-1.3 (-2.3-(-0.5))	0.382
Wits (mm)	0.3 (-1.0-1.5)	-1.2 (-2.6-0.0)	0.021
NSGn (°)	-0.3 (-1.5-0.8)	-0.5 (-1.9-0.2)	0.411
NAPg (°)	-0.7 (-3.5-0.7)	-2.2 (-4.9-(-0.4))	0.117
AnsPns/MeGo (°)	-1.3 (-3.1-0.6)	1.6 (-3.1-3.3)	0.085
SGo/NMe (%)	0.0 (0.0-0.1)	0.0 (0.0-0.0)	≤ 0.001
Björk's sum (°)	-3.0 (-5.1-(-0.6))	1.0 (-2.8-0.8)	0.037
Co-Gn (mm)	4.1 (2.4-5.3)	2.8 (0.4-6.4)	0.452
U1/Ans-Pns (°)	2.7 (-2.2-5.5)	4.9 (1.2-7.7)	0.087
L1/GoMe (°)	2.9 (-2.1-6.0)	-2.7 (-4.0-3.0)	0.046
U1/NA (mm)	2.7 (0.2-4.3)	-2.3 (-4.8-(-0.7))	< 0.001
L1/NB (mm)	1.4 (0.4-2.6)	-0.2 (-1.6-0.2)	< 0.001
OJ (mm)	-1.9 (-3.0-(-1.0))	-0.8 (-1.9-(-0.2))	0.027
Gl-Sn-Pg' (°)	0.2 (-3.0-2.4)	-1.0 (-2.9-0.4)	0.359

controls. In particular, a significant increase in the SNB angle and total mandibular length (Co–Gn) was observed, accompanied by a reduction in the ANB angle and Wits appraisal. Those findings support the concept that functional appliances can stimulate mandibular growth or redirect mandibular development when applied during an appropriate phase of skeletal maturation. Consistent with previous studies reporting enhanced mandibular advancement during the pubertal growth spurt (25,26), these changes may represent a temporary acceleration of mandibular growth; however, it cannot be excluded that growth subsequently slows.

The median increase in mandibular length in the treated group exceeded that observed in the matched control group (7.0 mm vs 2.8 mm), suggesting that the observed changes cannot be attributed solely to normal growth. A study by McNamara (32) demonstrated a greater mandibular response to functional orthopedic appliances in pubertal patients (8.7 ± 2.8 mm) compared to prepubertal patients (5.9 ± 2.3 mm), while untreated pubertal and prepubertal control groups showed increases of 4.8 ± 1.9 mm and 3.7 ± 1.1 mm, respectively. Those findings support the view that functional appliances used in growing patients may exert a true orthopedic effect rather than only dentoalveolar camouflage, regardless of appliance type. However, the issue remains controversial in the literature (9,14,31,32).

Cozza et al. (9) and Santamaria-Villegas et al. (33) found that the largest monthly increase in mandibular length occurred following use of the Sander bite-jumping appliance (0.34 mm per month) and the Herbst appliance (0.28 mm per month), followed by the Twin Block (0.23 mm per month), Bionator (0.17 mm per month), and Harvold Activator (0.12 mm per month). By contrast, the Frankel appliance produced the smallest increase, at 0.09 mm per month.

The absence of significant vertical changes further indicates that sagittal correction was achieved without unfavorable vertical growth patterns, which is clinically advantageous in Class II patients. The findings are comparable to those reported by Saikoski (34), Mills (35), and Soheilifar (36). The presence of acrylic bite ramps in functional appliances likely produces a bite-plane effect on posterior teeth, thereby improving vertical control.

In addition to skeletal effects, significant dentoalveolar changes were observed during the functional appliance phase. OJ decreased significantly as a result of mandibular advancement and dental compensation, including retroclination and retrusion of the maxillary incisors, and proclination and protrusion of the mandibular incisors.

Such dental changes align with previous findings (23,32,37) and are indicative of the functional appliances' mode of action and the loss of anchorage in the mandibular dentition (5). The retroclination of maxillary incisors observed in the study group may be explained by contact with lip musculature and the labial bow during functional appliance therapy. Toth and McNamara (37) also reported palatal tipping of the maxillary incisors caused by lip pressure during Twin Block treatment. Proclination of mandibular incisors may result from mesial forces acting on the mandibular incisors due to the forward positioning of the mandible, which is consistent with other studies (37). However, the magnitude of skeletal correction suggests that dental compensation alone does not explain the observed improvements.

The control group showed a slight decrease in OJ over time, which was not statistically significant and has also been reported in previous studies (23,28).

Effects of fixed orthodontic appliance therapy

The second phase of treatment with a fixed multibracket appliance and Class II elastics was primarily characterized by dentoalveolar changes. Although OJ continued to decline during this stage, the extent of skeletal change remained minimal and was not significantly different from that seen in the untreated control group.

The increase in Wits appraisal and the minimal change in SNB suggest a partial relapse or normalization of sagittal skeletal relationships during this phase, possibly related to growth patterns or dental decompensation associated with leveling and alignment mechanics.

Maxillary incisors showed a tendency toward protrusion during leveling and aligning using a fixed appliance. At the same time, lower incisor proclination and protrusion increased significantly due to use of Class II elastics. Class II elastics produce dental compensation rather than skeletal correction,

particularly after the peak growth period. These observations also support previous findings that skeletal gains achieved during functional appliance therapy may be partially masked during subsequent fixed appliance treatment if dental decompensation is not carefully controlled.

Vertical skeletal changes during the fixed appliance phase were minimal, although a significant decrease in Björk's sum suggested a tendency toward forward mandibular rotation. However, the changes were small and of uncertain clinical relevance. Importantly, no further enhancement in soft tissue facial convexity was detected during this phase, suggesting that the majority of the esthetic improvements occurred during the period of functional appliance therapy.

Soft tissue profile changes

Class II division 1 malocclusion affects facial profiles and aesthetics, often leading to concerns about appearance. The characteristic convex profile caused by mandibular retrusion creates an imbalance in facial proportions. Such aesthetic concerns can impact self-perception and social confidence, particularly in adolescents and young adults.

In our study, soft tissue analysis showed that functional appliance therapy significantly reduced facial convexity (Gl-Sn-Pg'), improving the facial profile. These findings are clinically relevant, as facial esthetics are often a primary concern for patients and parents seeking early treatment.

This improvement was maintained during the fixed appliance phase, although no further significant soft tissue changes were observed. The results emphasize the importance of early mandibular advancement in achieving favorable facial esthetics and highlight the clinical relevance of correcting skeletal discrepancies before final orthodontic detailing. Similar finding has also been reported in study by Singh and Clark (38).

Clinical implications

The findings of this study highlight the importance of treatment timing in Class II malocclusion with mandibular retrognathia. A two-phase treatment approach appears effective in achieving both skeletal correction and optimal dental occlusion in growing patients with Class II division 1 malocclusion. Functional appliances should preferably be used during the peak pubertal growth phase to achieve maximum mandibular advancement, while fixed appliances are mainly intended to complete occlusal correction and dental alignment.

Clinicians should be aware that some skeletal correction achieved during the first phase may be partially offset during the second phase due to dentoalveolar compensation. Therefore, careful treatment planning and biomechanical control are essential. Monitoring of lower incisor proclination is particularly important, as both treatment phases contributed to its increase, which may have implications for long-term periodontal health.

Additionally, this treatment approach may shorten overall treatment duration compared to conventional two-phase treatment in which removable functional appliances are used before puberty (approximately 2.3 years vs 3.4 years) (4,39,40). Furthermore, Giuntini et al. (4) reported shorter treatment durations with fixed appliances compared to combined treatment using fixed appliances and fixed functional appliances (1.2 years vs 2.3 years, respectively).

Limitations

Several limitations of this study should be acknowledged. First, the sample size was relatively small and derived from a single center, which may limit the generalizability of the findings. Second, the use of historical controls may introduce potential bias, despite matching for skeletal age and sex. Third, the study evaluated short-term treatment effects; therefore, long-term stability (e.g., 5 years) of skeletal and dental changes requires further investigation. Fourth, compliance with functional appliance wear was assumed but not objectively measured, which may have influenced the magnitude of the observed skeletal effects. Finally, LCs provide a two-dimensional assessment of three-dimensional structures, which may underestimate skeletal changes. Future studies incorporating three-dimensional imaging and long-term follow-up would provide additional insight into the stability of treatment outcomes. Notably, however, comparisons of one-phase vs two-phase treatment using new diagnostic tools and long-term stability has substantial clinical potential.

CONCLUSIONS

Treatment of Class II division 1 malocclusion using a functional appliance followed by fixed appliance therapy results in significant mandibular advancement, reduction in OJ, and improvement of facial profile. Skeletal changes occur primarily during the functional appliance phase, while fixed appliances contribute primarily to dental alignment and occlusal finishing. This two-phase treatment approach represents an effective strategy for managing growing patients with mandibular retrognathia, while balancing skeletal correction and esthetic outcomes.

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Obravnava venske golenje razjede pri bolnici v socialnovarstvenem zavodu: študija primera

Management of a Venous Leg Ulcer in a Resident Receiving Long-term Care: a Case Study

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Izvleček

Namen: *Venske golenje razjede so kronične rane, povezane s kroničnim venskim popuščanjem, ki pri starejših pomembno zmanjšujejo kakovost življenja, ter tudi povečujejo tveganje za okužbe in dolgotrajno oskrbo.*
Poročilo o primeru: *Predstavljamo študijo primera 82-letne bolnice, varovanke socialnovarstvenega zavoda z vensko golenjo razjedo leve noge. Obravnava je potekala od aprila do decembra 2024 ter je vključevala zdravljenje rane po načelih sodobne oskrbe (TIME), načrtovanje zdravstvene nege na podlagi temeljnih življenjskih aktivnosti in multidisciplinarno sodelovanje. Z individualizirano lokalno oskrbo kronične rane, učinkovitim obvladovanjem izločka, nadzorom vnetja in izločka, prehransko podporo, ustrezno analgezijo*

Abstract

Aim: *Venous leg ulcers are chronic wounds that are associated with chronic venous insufficiency, which significantly reduces the quality of life in elderly residents and increases the risk of infection and the need for prolonged care.*
Case Report: *We present a case involving an 82-year-old female resident of a long-term care facility with a venous leg ulcer on the left leg. Treatment was administered from April to December 2024 and included wound management according to modern care principles (tissue care, infection/inflammation control, moisture management, and epithelialisation support [TIME]), nursing care planning based on activities of daily living, and multidisciplinary collaboration. Complete*

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ter postopno aktivacijo v okviru fizioterapije smo dosegli popolno granulacijo in epitelizacijo rane. Ob zaključku obravnave bolečina ni bila več prisotna, izboljšalo se je spanje, zmanjšal se je strah pred amputacijo okončine ter izboljšalo se je psihološko počutje varovanke.

Zaključek: *Celostna, kontinuirana in interdisciplinarna obravnava starostnika z vensko golenjo razjedo v institucionalnem okolju lahko ob ustrezni izbiri oblog, kompresijski terapiji, nadzoru vnetja, podpori pri življenjskih aktivnostih vodi v uspešno zacelitev. Ključni dejavniki so realno zastavljeni cilji, redno vrednotenje poteka zdravljenja ter opolnomočenje bolnika in svojcev.*

wound healing with full granulation and epithelialisation was achieved through individualised local care of the chronic wound, effective exudate management, inflammation and exudate control, nutritional support, appropriate analgesia, and gradual mobilisation as part of physical therapy. At the conclusion of treatment, the pain had resolved, sleep had improved, the fear of limb amputation had decreased, and her psychological well-being had improved.

Conclusion: *Comprehensive, continuous, and interdisciplinary care of an elderly resident with a venous leg ulcer in an institutional setting can lead to successful healing with appropriate dressing selection, compression therapy, inflammation control, and support with activities of daily living. Key factors for a favourable outcome include realistic goal setting, regular evaluation of treatment progress, and empowerment of the resident and the family.*

INTRODUCTION

The population in Slovenia and worldwide is ageing, resulting in an increased prevalence of chronic diseases and conditions associated with chronic wounds. Venous leg ulcers (VLUs) are the most common type of chronic lower limb ulcer and are closely linked to venous hypertension and chronic venous disease (1,2). LUs arise from venous valve dysfunction and venous reflux, which leads to sustained venous hypertension, inflammation, and subsequent tissue damage. Clinically, this pathophysiologic process presents as an ulcer that is most often situated in the lower one-third of the leg (2,3). VLUs typically require several months to heal and have a high recurrence rate, underscoring the importance of secondary prevention after wound closure (4-10).

VLUs have a significant impact on the physical and psychological well-being of residents in long-term care facilities and are associated with pain, reduced mobility, sleep disturbances, malodour, social isolation, and fear of complications (5–7). In institutional settings, further challenges arise due to multimorbidities, immobility, and dependence on assistance with activities of daily living. However, detailed reports describing comprehensive interdisciplinary management of VLUs in frail residents of long-term care institutions remain limited in the literature.

The aim of this case study is to present a comprehensive approach to managing a resident with a VLU in a social welfare institution and to highlight the key multidisciplinary interventions that contributed to successful wound healing.

CASE PRESENTATION

The principles of the CAse REport (CARE) guidelines were followed in preparing this case presentation. Personal data have been anonymised and are presented only to the extent necessary for clinical understanding of the case.

Resident Data and Medical History

The case involves an 82-year-old female resident in a social welfare institution with a VLU on the left lower limb that was present since 2022 and characterised

by multiple ulcerative areas. The medical history includes advanced chronic venous insufficiency, arterial hypertension, and osteoporosis.

In 2022 she was hospitalised for infection of chronic venous ulcers on the pre-tibial skin bilaterally. The ulcers on the pre-tibial skin persisted after discharge but no signs of acute inflammation were observed during the follow-up examination. Regular dressing changes were recommended every 3–4 days with additional home phototherapy using a light source (Bioptron®, Zepter International, Wollerau, Switzerland) during dressing changes.

In the following months the ulcer on the right pre-tibial skin was more painful than the left pre-tibial skin. An above-knee amputation of the right lower limb was performed in September 2023 due to recurrent infections of the ulcers and the development of critical ischaemia of the right lower limb. The procedure had a significant impact on her functional status and psychological condition, particularly in terms of reduced mobility and increased anxiety about the outcome of the disease.

Post-amputation the resident exhibited immobility and severe functional dependence. Care was provided at home with the support of a community nurse and caregivers before institutionalisation. She was admitted to a social welfare institution in March 2024 as her need for round-the-clock assistance increased. Upon admission, the resident required assistance with all basic activities of daily living, including personal care, mobility, transfers, and toileting. The greatest functional limitation was her inability to move independently because she was unable to use a wheelchair effectively due to the right limb amputation.

During care, she experienced appetite disturbances, occasionally refused food, and showed reduced motivation to participate actively in physiotherapy. During dressing changes, when the wound dressings listed in Table 2 were used, she reported burning and tearing pain, expressed fear of possible amputation of her left lower limb, and suffered from insomnia. We assessed her sleep disturbances using the Insomnia Severity Index [ISI] (range, 0–28), which categorises insomnia as follows: 0–7, no clinically significant insomnia; 8–14, subclinical insomnia; 15–21, moderate clinical insomnia; and 22–28, severe insomnia. The resident scored 20/28 on the ISI at the time of admission, indicating moderate clinical insomnia. Upon completing treatment, she scored 6/28 on the ISI, which was consistent with the absence of clinically significant insomnia and a subjective improvement in sleep quality.

Table 1: *Clinical characteristics of the resident*

Gender/age	Female, 82 years
Accommodation	Long-term care facility
Diagnosis	Venous leg ulcer of the left lower leg (history of bilateral ulcers since 2022); chronic venous insufficiency
Clinical description of the ulcer	
	Venous leg ulcer with multiple ulcerative areas; shallow lesions without necrosis; during exacerbation, increased exudate and unpleasant odour
Mobility and cooperation	Immobile; dependent on assistance due to above-knee amputation of right leg
Key challenges	Pain, insomnia, fear of amputation, decreased appetite, limited activity

Initial assessment of the wound

According to Falanga's classification of wound bed preparation, which combines wound appearance (A–D) and exudate control (1–3), the ulcer was assessed as C3 at the start of monitoring [< 50% granulation tissue, fibrin coating present, no eschar; uncontrolled exudate requiring daily dressings] (11). Upon completing treatment, the wound was classified as A1 (100% epithelialisation and controlled exudate). At the start of the observation period (April 2024), the VLU on the left pre-tibial skin was characterised by multiple ulcerative areas of varying size, covered with fibrin deposits and a profuse exudate. The wound edges were covered with non-viable epithelial debris and the surrounding skin was dry and scaly. Minor bleeding occurred during dressing changes. The multiple ulcerative areas noted were clinically assessed as part of a single VLU.

Compression Therapy

Compression was gradually introduced according to the resident's tolerance with regular monitoring of pain, the condition of her skin, and signs of potential ischaemia as part of standard safety procedures during compression therapy. The aim was to achieve a therapeutic pressure of approximately 30–40 mmHg at the ankle with a gradual reduction proximally. Bandages were applied after wound cleansing and dressing changes (every 1–2 days or daily if the condition worsened).

After a reduction in oedema and exudate and subsequent wound stabilisation, complete wound healing with full granulation and epithelialisation was achieved. Following ulcer healing, compression therapy was continued using class II elastic compression stockings (23–32 mmHg; Sigvaris AG, St. Gallen, Switzerland) as a secondary preventive measure to reduce the risk of recurrence.

The resident and her family were instructed on the importance of regular compression therapy, leg elevation at rest, and daily skin inspection.

NURSING CARE PLAN AND INTERVENTIONS

Based on a comprehensive initial assessment, an individualised care and treatment plan was developed in accordance with the principles of multidisciplinary care. The plan was prepared and implemented with the involvement of a physician, registered nurses, a physiotherapist, an occupational therapist, social services, and family members, who participated in defining care goals, supporting the resident, and monitoring progress.

Local wound care, pain management with analgesics, insomnia management with sedatives, nutritional support, prevention of immobility complications, such as risk of contractures, pressure ulcers, and infectious complications, and gradual functional activation were prioritised according to the abilities and tolerance of the resident. Local wound care was performed according to the principles of tissue care, inflammation/infection control, moisture management, and epithelialisation support (TIME) approach, ensuring coordinated treatment of local and systemic factors affecting the healing process through interdisciplinary cooperation.

Treatment progress was regularly evaluated at team meetings, where nursing and therapeutic measures were adjusted as needed based on the clinical response of the wound, pain intensity, functional status, and resident cooperation.

Table 2: *Timeline and key actions (April to December 2024)*

April 2024	Initial assessment, wound cleansing with tap water and mild soap (17), application of advanced dressings according to exudate level, and compression therapy as tolerated; Provision of analgesia prior to dressing changes; Monitoring fluid balance and supporting adequate nutritional intake through regular nursing assessment, including encouragement of protein- and energy-rich meals.
May - Avgust 2024	Regular dressing changes every 1–2 days, with dressing selection based on wound characteristics, including absorptive dressings (alginate, polyurethane foam), antimicrobial dressings (copper oxide–impregnated), and protective/occlusive dressings (polyester film).
October 2024	Additional support for healing was provided by polarized light phototherapy, alongside continuation of standard care and gradual mobilization.
December 2024	Complete granulation and healing of VLU achieved; no pain; reduced fear and improved cooperation in care and rehabilitation.

RESULTS

The VLU was in the complete granulation phase after 8 months (from April 2024 to December 2024) and had healed by mid-December 2024. The resident reported that the pain had resolved and she was sleeping better at night. Her psychological state improved with a reduced fear of amputation and increased willingness to participate in the physiotherapy programme.

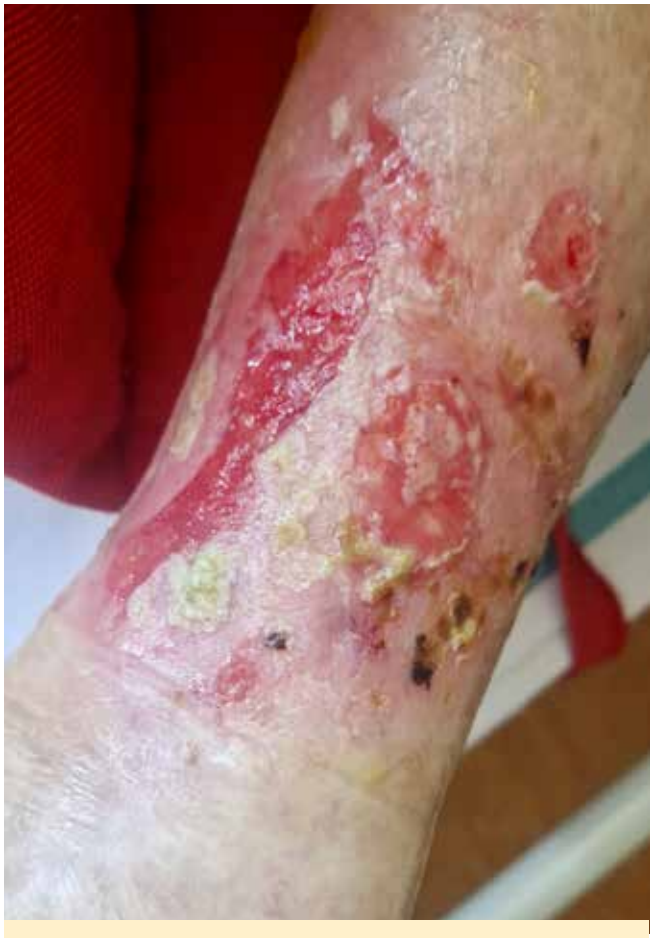

Figure A: *Presentation of the initial clinical condition of the venous leg ulcers (VLCs) with multiple ulcerative areas before the introduction of light therapy (April 2024).*

DISCUSSION

VLUs are caused by chronic venous disease and venous hypertension and represent a significant burden for residents and the healthcare system (1,2,9). In the case presented herein, in addition to the local wound, accompanying factors were crucial: advanced age; immobility due to amputation; incontinence; decreased appetite; pain; insomnia; and psychological stress.

Systematic wound assessment and adaptation of local care are the foundation of effective treatment in chronic wounds. The TIME concept enables structured decision-making regarding debridement, infection control, moisture management, and promotion of epithelialization (8).

The Falanga classification in the assessment was also included for a more objective and repeatable description of the wound bed. This classification combines the appearance of the wound (proportion of granulation and presence of fibrin or eschar) and the degree of exudate control, enabling clearer monitoring of progress and communication within the team (10).

Compression therapy remains the primary intervention for VLU but in practice the effectiveness is often limited by resident tolerance, mobility, and cooperation (12,13). In an institutional setting it is crucial to gradually introduce compression and regularly assess the skin and pain.

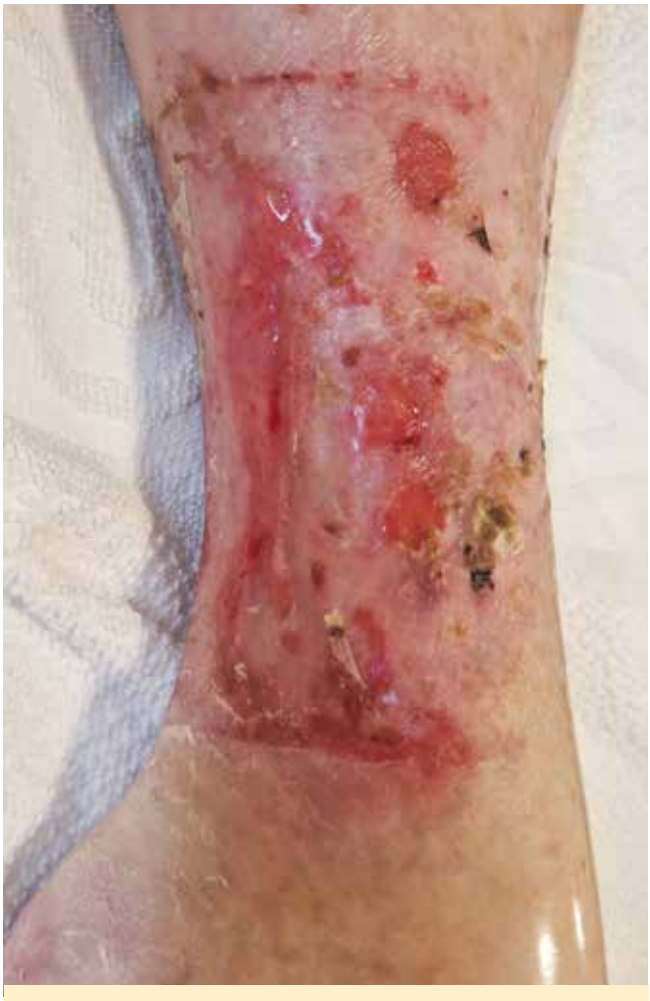

Figure B: *Presentation of the clinical condition of VLUs after 2 months of treatment (June 2024).*

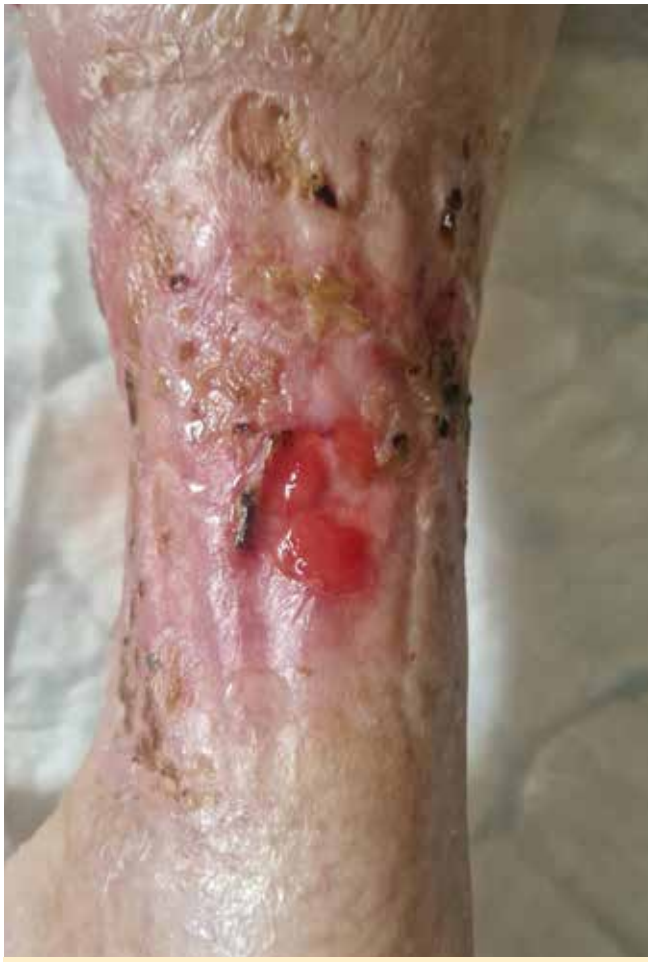

Figure C: *Presentation of the clinical status of VLUs after adjuvant phototherapy (October 2024).*

Nutrition and nutritional status have a significant impact on wound healing outcomes. Evidence supports the importance of adequate protein and micronutrient intake (e.g., vitamin C and zinc), while malnutrition is associated with delayed healing and increased complications (11). In the case herein, nutritional support included encouraging regular energy- and protein-rich meals, providing oral nutritional supplements enriched with protein, vitamins, and trace elements due to reduced appetite, and regularly monitoring fluid intake with nursing staff offering assistance and encouragement during meals. Residents with reduced appetite require active monitoring of intake and early intervention with individualised dietary adjustments.

Insomnia was systematically monitored using the ISI scale because sleep disturbances significantly affect regeneration, pain tolerance, and cooperation during treatment. Regular assessment allowed adjustment of non-pharmacologic measures (sleep hygiene and structuring of daily activities), and, if necessary collaboration with a physician to optimize therapy (14).

VLU-associated pain is often complex, combining chronic and procedural elements, and can lead to sleep disturbances and reduced cooperation in treatment (6,7). In the case herein, analgesia before dressing changes and psychological support due to fear of amputation were important. Quality of life in residents with chronic wounds is often an overlooked outcome, although quality of life significantly affects cooperation and long-term success (5).

Figure D: *Photography of the healed VLUs after 8 months of treatment (December 13, 2024).*

Physical activity is limited in individuals with VLUs due to pain and poor muscle pump function but structured exercise with compression can benefit the healing process (15-17). Realistic goals are less ambitious (e.g., active exercises in bed, short-term mobilization, and transfer to a wheelchair with the help of healthcare staff) for immobile residents but these measures are also important for preventing complications of immobility and psychological well-being.

In recent years, complementary methods (i.e., biophysical interventions, including phototherapy) have also been used (18,19). However, there is still insufficient evidence to support the routine use of complementary methods and are generally applied as an adjunct to standard care. In the case herein, polarised light phototherapy (Bioptron) was used as an adjunctive intervention with standard wound care. Infection was not clinically confirmed in the case herein. Therefore, management focused on controlling inflammation and prevention, including regular wound assessment, appropriate dressing selection (e.g., absorptive and antimicrobial dressings, as indicated), and strict hygiene during dressing changes (20).

Nutritional support included encouragement of regular energy- and protein-rich meals with oral nutritional supplements enriched with protein, vitamins, and trace elements due to the resident's reduced appetite.

Family members were actively involved in the care process, particularly in providing psychological support, encouraging adherence to treatment (e.g., compression therapy and nutrition), and participating in care planning and education provided by the healthcare team.

Overall, phototherapy served as a supportive and motivational intervention, while the primary drivers of healing were standard evidence-based measures, including local wound care, compression therapy, nutritional support, and rehabilitation.

The limitation of this case study was that the results cannot be generalized. Nevertheless, the case highlights the importance of continuous nursing care, structured assessment, teamwork, and resident empowerment in an institutional setting.

CONCLUSION

This case demonstrates that healing is possible in an elderly resident with a venous leg ulcer in a social care institution, even with multiple limitations, such as advanced age, immobility, pain, and psychological distress, if the treatment is comprehensive, individualized, and continuous. The key factors for success were regular wound assessment and adjustment of care according to TIME principles, effective inflammation and exudate control, nutritional support, pain management, appropriate tolerance-based compression therapy, and multidisciplinary rehabilitation. Psychological support and involvement of family members also had important roles in treatment.

This case contributes to the existing literature by illustrating the practical implementation of comprehensive VLU management in a long-term care setting, where treatment is often complicated by immobility, multimorbidity, functional dependence, and psychological distress. The report highlights the importance of integrating evidence-based wound care, compression therapy, rehabilitation, nutritional support, and psychosocial interventions to achieve successful healing outcomes in frail older adults. Furthermore, it emphasises the value of continuous interdisciplinary collaboration and individualised care planning in institutional care environments.

CONFLICT OF INTEREST

The authors declare that no conflict of interest exists.

FUNDING

The study received no funding.

ETHICAL APPROVAL

No approval by the National Medical Ethics Committee was necessary to conduct the study due to the selected research methodology.

AUTHOR CONTRIBUTION

The authors independently carried out the entire research process, including literature search and analysis. They also wrote the entire manuscript and conducted the final revision of the article. The authors confirm that they are solely responsible for all aspects of the research and writing.

PATIENT CONSENT FOR PUBLICATION

The patient has provided written informed consent and agrees to the publication of the article describing her case.

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Fournierjeva gangrena pri ženski bolnici: prikaz primera

Fournier's Gangrene in a Female Patient: a Case Report

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Fournierjeva gangrena, ženska, nekrotizirajoč fasciitis, prikaz primera, multidisciplinarni pristop

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Izvleček

Namen: *Fournierjeva gangrena (FG) je redka, življenje ogrožujoča oblika nekrotizirajočega fasciitisa, ki se pojavi na spolovilu, perinealnem in perianalnem predelu. Pri ženskah ugotavljamo bistveno višjo stopnjo umrljivosti zaradi anatomskih razlik in večje dovzetnosti za peritonitis in retroperitonitis. Pogosti dejavniki tveganja vključujejo sladkorno bolezen, zlorabo substanc, jetrno odpoved in imunosupresijo (1–4).*

Prikaz primera: *73-letna gospa je bila pripeljana v urgentni center zaradi kolapsa, tahikardije in atrijske fibrilacije. Ob pregledu so ugotovili, da je bila gospa isti dan že obravnavana pri izbranem ginekologu zaradi otečenih, pordelih in bolečih levih*

Abstract

Aim: *Fournier's gangrene is a rare life-threatening form of necrotizing fasciitis that affects the genital, perineal and perianal regions. A significantly higher mortality rate occurs in females due to anatomic differences and greater susceptibility to peritonitis and retroperitonitis. Common risk factors for Fournier's gangrene include diabetes melitus, substance abuse, liver failure, and immunosuppression.*

Case presentation: *A 73-year-old woman collapsed and was transported to the emergency room tachycardic and in atrial fibrillation. Earlier that day she had an appointment with her gynecologist for evaluation of an inflamed, er-*

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sramnih ustnic, za kar je izbran ginekolog predpisal antibiotično terapijo.

ythematous, painful left labia, which the gynecologist treated with antibiotics.

INTRODUCTION

Fournier's gangrene (FG) is a form of necrotizing fasciitis with a 20% mortality rate. FG primarily affects males > 50 years of age with a male-to-female ratio of 10:1. Despite the lower incidence, females have a higher mortality due to anatomic factors and a greater risk of peritonitis and retroperitonitis. FG affects the external genitalia, perineum, or perianal regions. FG is typically a polymicrobial infection. Cultures obtained from affected sites frequently grow *Staphylococcus spp.*, *Streptococcus spp.*, *Escherichia coli*, *Pseudomonas spp.*, *Bacteroides spp.*, and non-bacterial *Candida spp.* The common symptoms associated with FG include swelling of the external genitalia, pain, and a high fever. A delay in diagnosis after symptom onset can lead to skin necrosis. Erythema can progress along anatomic fascial planes. Due to the high mortality rate, immediate surgical intervention and broad-spectrum antibiotics are indicated (1-6).

CASE PRESENTATION

A 73-year-old woman with type 2 diabetes mellitus and paroxysmal atrial fibrillation collapsed and was transported to the emergency room tachycardic and in atrial fibrillation. Earlier that day she had an appointment with her gynecologist for evaluation of an inflamed, erythematous, painful left labia majora, which she noted after expressing the contents of a pustule. An ultrasound showed no evidence of an abscess, therefore the gynecologist cleaned the wound and prescribed antibiotics.

The left labia were severely swollen and sensitive to touch with a visible protrusion from which there was a purulent drainage. Furthermore, erythema of the gluteal and upper thigh areas was visible (Fig. 1).

In addition to a CT scan, blood cultures and a swab of purulent discharge were ordered. The CT scan showed thickening of the skin, structurally modified subcutaneous fat tissue on the left side of the mons pubis, outer labia, and perineum, and minimal extension to the gluteal area. The tissue changes extended to the superficial muscle fascia without air inclusion and liquid collection in the deeper tissues (Fig. 2).

Figure 1: *Swelling and erythema of the genital and upper thigh areas.*

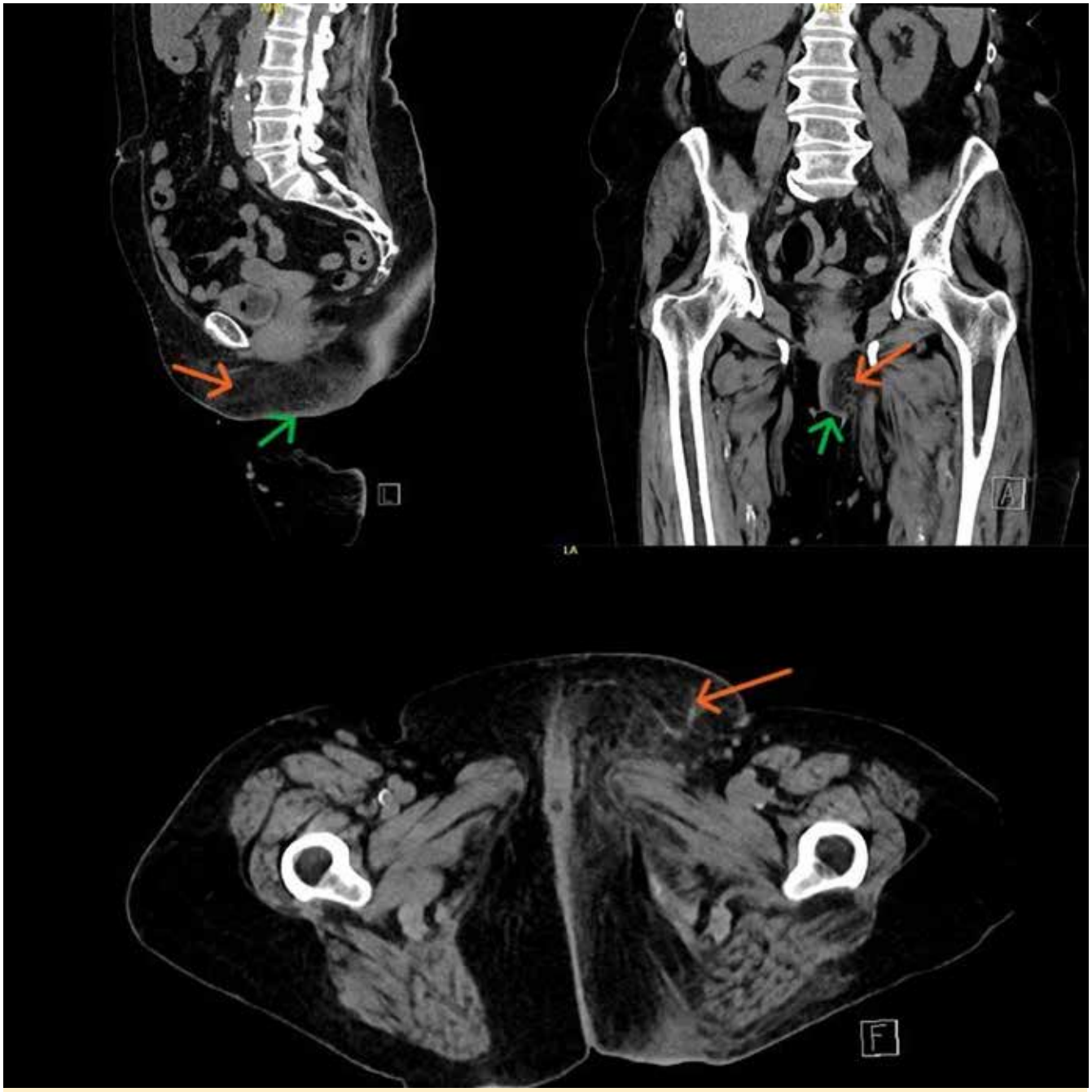

Figure 2: *A CT scan of the pelvis and lower abdomen shows thickened skin (green arrows), structurally altered subcutaneous fat of the left mons pubis, left labia majora, and left perineum with minimal extension to the left gluteal area (orange arrows).*

Because the CT scan was suspicious for FG, the patient was treated with empiric antibiotics (clindamycin and ceftriaxone). Moreover, incision and drainage was performed under local anesthesia, which yielded a purulent outflow. The patient was subsequently admitted to the intensive care unit in septic shock, where she received vasoactive therapy.

The blood culture results were negative, while the swab of the purulent drainage was positive for *E. coli*, *Enterococcus faecalis*, *E. avium*, *Streptococcus dysgalactiae*,

Bacteroides ovatus, *Actinomyces turicensis*, *Atopobium minutum*, and *Fusobacterium nucleatum*.
The patient was transferred to the Gynecology Department when hemodynamically stable,where spreading of the erythema and swelling was noted and the area was severely painful. Skin necrosis was present on the upper inner area of the thigh and lower gluteal area on the left side, measuring 3 x 3 cm (Fig. 3).

An MRI showed multiple abscesses within the muscles of the left thigh, so surgical treatment was indicated (Fig. 4). Ceftriaxone was replaced by piperacillin with a beta-lactamase inhibitor.

Figure 3: *Widespread erythema and swelling with skin necrosis.*

Surgical treatment entailed excision of the necrotic skin and subcutaneous tissue, evacuation of abscesses, and irrigating the wound with hydrogen peroxide. Swabs were obtained for microbiological testing. The excisions were revised in the ensuring days and a biopsy of necrotic tissue was obtained. The biopsy confirmed the diagnosis of necrotizing fasciitis. The swelling and erythema in the inguinal area on the left side increased 4 days postoperatively, therefore another incision was performed. In addition, a terminal sigmoidostomy was performed. Regular wound dressings were changed in the following 2 weeks and the patient's condition improved significantly. She was discharged to home with instructions for stoma care and a referral to a home care service.

DISCUSSION AND CONCLUSION

FG progresses rapidly and is often misdiagnosed due to non-specific symptoms, such as fever, perineal edema, and pain. As FG continues to progress, crepitus, a purulent discharge, and necrosis become apparent. A clinical diagnosis is made based on physical findings, imaging, risk factors, and standardized scoring. The most common risk factor for FG is diabetes melitus; other risk factors include substance abuse, liver failure, and immunosuppression. Treatment of FG includes immediate surgical intervention and broad-spectrum antibiotics (7-9).
This case demonstrated the rapid progression of FG and therefore highlights the importance of a multidisciplinary treatment approach. It is essential to rule out FG when a patient presents with the aforementioned symptoms and has multiple risk factors. It is recommended to monitor these patients closely, obtain swabs and blood cultures as soon as FG is suspected, order imaging, and consult infectious disease specialists and surgeons for timely intervention (7-10).

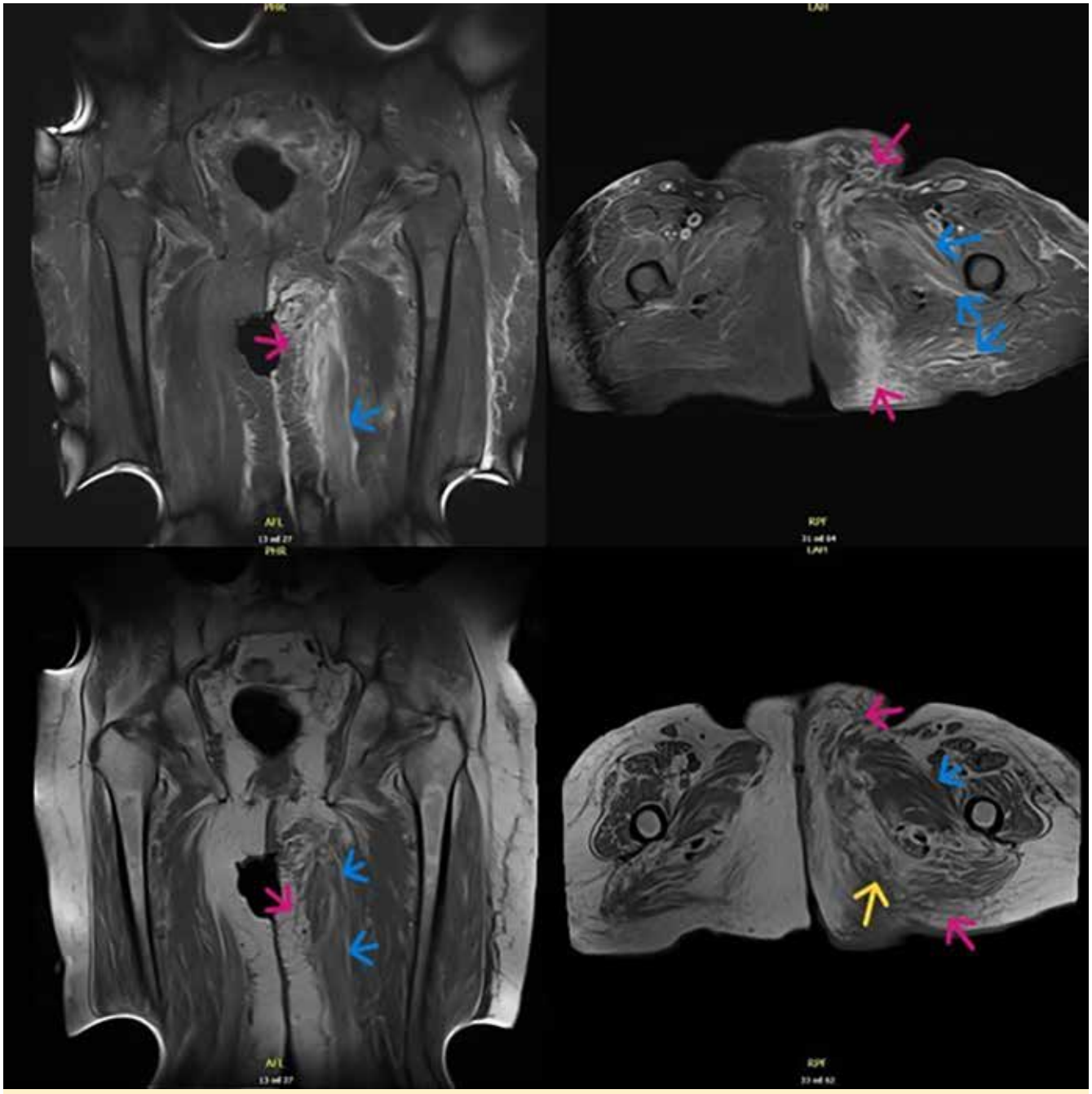

Figure 4: *MRI of the pelvis shows cellulitis on the inner and dorsal aspects of the left thigh (pink arrows) and fluid collection in the labia on the left, lateral to the left gracilis muscle (yellow arrows). Additionally the MRI shows mild-to-moderate thickening of the superficial and deeper fascia (blue arrows).*

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Katetrska ablacija atrijske fibrilacije pri bolnikih s cor triatriatum sinister: opis primera in pregled literature

Anatomical Considerations Regarding Catheter Ablation of Atrial Fibrillation in Cor Triatriatum Sinister: A Case Report and Review of the Literature

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Izvleček

Uvod: *Cor triatriatum sinister (CTS) spada med redke prirojene srčne napake. Katetrska ablacija atrijske fibrilacije (AF) pri pacientih s CTS zahteva ustrezno predoperativno pripravo zaradi anatomskih posebnosti.*

Predstavitev primera: *49-letna bolnica z znanim CTS je bila sprejeta v našo ustanovo za katetrsko ablacijo paroksizmalne AF. Ultrazvok srca je prikazal razširjen levi preddvor, ki je bil s tanko membrano razdeljen na dve ločeni votlini. Magnetnoresonančno slikanje srca je razkrilo dodatno membrano pred levimi pljučnimi venami. Poseg smo opravili pod nadzorom znotrajsrčnega ultrazvoka in fluoroskopije. Izdelali smo elektro-anatomsko mapo levega preddvora in električno izolirali desne pljučne vene. Levih pljučnih ven nismo uspeli*

Abstract

Introduction: *Cor triatriatum sinister (CTS) is a rare congenital cardiac defect. Catheter ablation of atrial fibrillation (AF) in patients with CTS has important anatomical considerations.*

Case presentation: *A 49-year old female patient with a known CTS was referred to our institution for catheter ablation of symptomatic paroxysmal AF. Echocardiography revealed a dilated left atrium, which was split into two separate compartments by a thin fibromuscular membrane. A second membranous structure, in front of the left pulmonary vein (PV) ostia, was noted on the preprocedural magnetic resonance scan. The procedure was guided by intracardiac echocardiography and fluoroscopy. A 3D-electroanatomic map was created and the*

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mapirati in izolirati. V več kot enem letu spremljanja po posegu, bolnica simptomov motnje ritma ni več zaznala.

Diskusija: *Katetrska ablacija AF predstavlja uporabno metodo za dolgotrajno vzdrževanje sinusnega ritma pri bolnikih s CTS. V pregledani literaturi so se avtorji pri tej populaciji najpogosteje osredotočili na slikovno diagnostiko ali pred ali med posegom, ter tudi na različne strategije katetrske ablacije. Dodatna membrana pred levimi pljučnimi venami zaenkrat še ni bila opisana.*

right PVs were isolated. The left PVs could not be mapped and isolated. The patient was discharged the following day without complications, and has remained entirely asymptomatic for over one year.

Discussion: *Catheter ablation in patients with AF and a CTS appears to be a feasible rhythm control treatment modality. Most published literature details preprocedural and intraprocedural CTS assessment with different imaging modalities, as well as different ablation strategies based on the arrhythmia type. To the best of our knowledge, an additional membranous structure in front of the left PVs has not been reported.*

INTRODUCTION

Cor triatriatum sinister (CTS) is a rare cardiac anomaly that accounts for approximately 0.1% - 0.4% of congenital cardiac diseases (1). The left atrium is divided into two compartments by a thin fibromuscular membrane. The incidence of atrial fibrillation (AF) in CTS is estimated at around 30% (2). Here, we present a patient with a CTS who underwent catheter ablation for symptomatic paroxysmal AF, and provide a review of the literature regarding catheter ablation in patients with a CTS.

CASE PRESENTATION

A 49-year old female Caucasian patient was referred to our electrophysiology section for catheter ablation of symptomatic paroxysmal AF. At the time of admission, the patient reported episodes of self-limited dyspnea, fatigue and palpitations, lasting for several hours. An electrocardiogram revealed normal sinus rhythm. Transthoracic echocardiography (TTE) showed a mildly dilated left ventricle, normal ejection fraction, and no significant valvular pathologies. The left atrium (LA) was dilated (LAVI = 67 ml/m2) and split into two separate compartments by a thin membrane. Transesophageal echocardiography (TEE) revealed a thin fenestrated fibromuscular membrane that extended from the fossa ovalis to the Coumadin

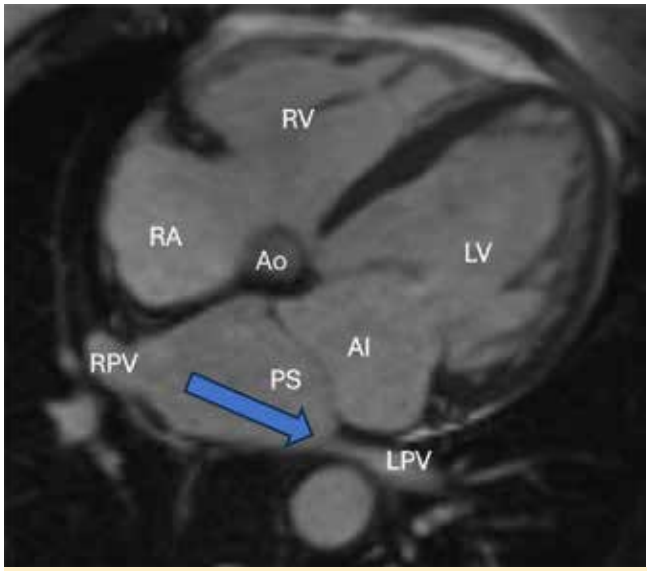

Figure 1: *A 4-chamber view of the cardiac magnetic resonance scan, which shows both compartments of the left atrium. The arrow points towards the second membranous structure, in front of the left pulmonary vein ostium.*

RV – right ventricle, RA – right atrium, LV – left ventricle, Ao – ascending aorta, AI – anteroinferior compartment of the left atrium, PS – posterosuperior compartment of the left atrium, LPV – left pulmonary vein, RPV – right pulmonary vein

ridge. It divided the LA into a posterosuperior section containing pulmonary vein (PV) ostia, and an anteroinferior compartment with the left atrial appendage and the mitral annulus. No significant gradient was noted at the level of the membrane. Cardiac magnetic resonance imaging (MRI) confirmed the position and benign nature of the membrane. Furthermore, a second thin membrane, in front of the left PV ostia, was noted (Figure 1). The left PVs were not dilated and there were no signs of pulmonary congestion.

The procedure was performed in the electrophysiology laboratory under conscious sedation. The patient signed informed consent. Three right femoral vein punctures were performed. A decapolar mapping catheter was placed in the coronary sinus and an intracardiac echocardiography (ICE) probe was placed in the high right atrium. Transseptal puncture (TSP) was guided by fluoroscopy and ICE, and the long sheath was placed in the posterosuperior compartment. A focal contact-force sensing irrigated ablation catheter was inserted and electroanatomic (EAM) mapping was performed (Figure 2). Right PVs were tagged. Left PVs could not be accessed and mapped from the posterosuperior compartment, due to the second membrane. Blood flow from the left PVs towards the posterosuperior compartment of the LA was confirmed with color Doppler on ICE.

Wide antral circumferential point-by-point radiofrequency ablation of the right PVs was performed and was guided by ablation-index (450 on the anterior wall and roof, and 300-350 on the posterior and inferior walls). Bidirectional block to the right PVs was verified. No residual electrograms inside the right PV ostia were observed (entrance block). Exit block was confirmed by a lack of LA capture during high-output pacing maneuvers performed from the inside of the right PVs. A second TSP to the anteroinferior part of the LA could not be performed because the fossa ovalis was oriented entirely towards the posterosuperior chamber. The patient was discharged the following day without complications on antiarrhythmic pharmacotherapy consisting of a low-dose class Ic agent in combination with a beta-adrenergic blocker. A routine outpatient follow-up was scheduled at 12 months.

At follow-up, the ECG demonstrated sinus rhythm and the patient reported no AF-related symptoms.

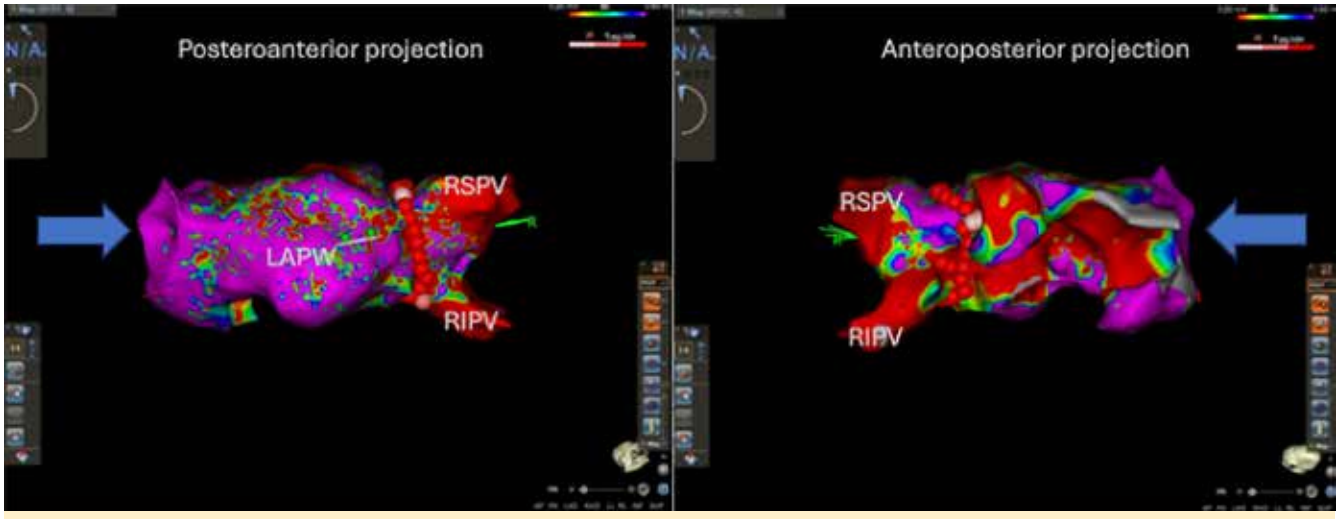

Figure 2: *A 3D-electroanatomic map (posteroanterior projection on the left side and anteroposterior projection on the right side) of the posterosuperior compartment in the left atrium. The arrow points towards a second membranous structure, which prevented mapping of the left pulmonary veins.*

RSPV – right superior pulmonary vein, RIPV – right inferior pulmonary vein, LAPW – left atrial posterior wall

Accordingly, antiarrhythmic therapy was discontinued. Anticoagulation with a direct oral anticoagulant (DOAC) was resumed indefinitely given a CHA2DS2-VA score of 2.

DISCUSSION

Catheter ablation for AF in a patient with a CTS was first described in 2008 (3). Fifteen case reports and two case series (Table 1) have been published to date (2-18). Several reports focused on detailed preoperative imaging techniques (6,9,11,13,17,18) and the utility of ICE or TEE-guided TSP (4,5,7,12,13,15,18). Anatomical considerations for catheter ablation of atrial tachyarrhythmias in patients with CTS were discussed in some studies (4,7,14,15). Coexistence of CTS and other congenital cardiac variations was reported (7,14,15,16). Furthermore, different ablation strategies and modalities were explored in several studies (2,5,8,10,16,17). In summary, catheter ablation has been reported as a feasible rhythm-control strategy in patients with CTS and AF. Nevertheless, meticulous preprocedural anatomic characterization using TTE, TEE, and cardiac CT or MRI is crucial given the altered atrial anatomy associated with CTS. Our case of catheter ablation in a patient with a CTS was similar to previous reports in certain aspects. The LA was split into the posterosuperior section

Table 1: *Procedural characteristics of catheter ablation for left atrial tachyarrhythmias in patients with cor triatritum sinister in our report and in the existing literature.*

Case report/ Case series	Indication	Preprocedural imaging	Guidance of ablation	Transseptal puncture	Ablation targets	Additional information
Yamada et al, 2008 (3)	Paroxysmal AF	TTE, TEE,	Fluoroscopy, 3D EAM	TSP into anteroinferior chamber; ablation catheter looped back through CTS membrane into posterosuperior chamber	PV isolation	First description of AF ablation in CTS; highlighted the need for precise imaging to perform posterior TSP into PV-containing compartment.
Bhatia et al, 2010 (4)	Persistent AF	TTE, CT scan	Fluoroscopy, ICE, 3D EAM (combined with ICE images)	TSP into posterosuperior chamber (ICE-guided)	PV isolation	Feasibility of ICE-guided TSP.
Gavin et al, 2011 (5)	Persistent AF	TTE, CT scan	Fluoroscopy, TEE, 3D EAM	TSP into posterosuperior chamber (TEE-guided)	PV isolation, roof line, mitral isthmus line, complex fractionated electrogram ablation	Feasibility of TEE-guided TSP; complex ablation procedure in both compartments of LA.
Fukumoto et al, 2012 (6)	Paroxysmal AF	TTE, TEE, CT scan	Fluoroscopy, ICE, 3D EAM (merged with CT scan)	TSP into posterosuperior chamber (ICE-guided)	PV isolation	Merging 3D EAM with CT scan in CTS.
Tokuda et al, 2016 (7)	Persistent AF	TTE, CT scan	Fluoroscopy, ICE, 3D EAM	No TSP, access to posterosuperior compartment obtained via patent foramen ovale	Left common trunk and right PVs isolation, box lesion in posterior LA	Coexistent CTS and left common PV trunk.

Case report/ Case series	Indication	Preprocedural imaging	Guidance of ablation	Transseptal puncture	Ablation targets	Additional information
Borne et al, 2016 (8)	AF and macroreentrant AT (perimitral, roof-dependent, CTI-dependent flutter)	TTE, TEE, CT scan	Fluoroscopy, ICE, 3D EAM	TSP into posterosuperior chamber (ICE-guided)	PV isolation, roof line, mitral isthmus line, CTI line	Sequential treatment of AF and multiple macroreentrant ATs in CTS.
Paelinck et al, 2018 (9)	Paroxysmal AF	TTE, CT scan	Fluoroscopy, TEE, 3D EAM	TSP into posterosuperior chamber (TEE-guided)	PV isolation	/
Shah et al, 2018 (10)	Long-standing persistent AF	TTE, TEE, CT scan	ICE and 3D EAM	TSP into posterosuperior compartment (ICE-guided)	PV isolation	Zero-fluoroscopy ablation in CTS.
Morishima et al, 2020 (11)	Paroxysmal AF	TTE, CT scan	Fluoroscopy, ICE and 3D EAM (merged with ICE images)	TSP into posterosuperior chamber (ICE-guided)	PV isolation, SVC isolation	/
Okada et al, 2020 (12)	Macroreentrant atrial tachycardia (incorporating fibromuscular membrane)	TTE, CT scan	Fluoroscopy,ICE and 3D EAM	TSP into posterosuperior chamber (ICE-guided)	PV isolation, SVC isolation, ablation of fractionated potentials on the membrane	Figure-of-8 re-entry using CTS membrane as a critical isthmus.
Lugtu et al, 2021; case series (13)	AF or macroreentrant AT (4 patients; case series)	TTE, CT scan	Fluoroscopy, 3D EAM (merged with cardiac CT)	TSP into posterosuperior chamber (TEE or fluoroscopy-guided)	PV isolation (4 patients), roof-line and a line from the membrane to the roof-line (1 patient)	Fractionated potentials on the fibromuscular membrane.
Karimianpour et al; case series 2021 (2)	AF (four patients; case series), macroreentrant atrial tachycardia (one patient)	TTE, TEE (2 cases), CT scan	Fluoroscopy, ICE, 3D EAM	TSP into posterosuperior chamber (ICE-guided)	PV isolation (4 patients), roof-line, mitral isthmus line, ablation of fractionated potentials next to the membrane (1 patient)	CTS present in 0.1% of AF ablation refferals; reisolation of PVs in recurrent AF is feasible.
Minciuna et al, 2022 (14)	Persistent AF	TTE, CT scan	Fluoroscopy, TEE, 3D EAM	TSP into posterosuperior chamber (TEE-guided)	Left common trunk and right PVs isolation; high-power short-duration RF energy.	Catheter stability issues when ablating on common trunk near the CTS membrane.
Iwata et al, 2022 (15)	Persistent AF	TTE, TEE, CT scan	Fluoroscopy, TEE, 3D EAM	TSP into posterosuperior chamber (TEE-guided)	PV isolation and SVC isolation	Coexistent CTS and ASD, feasibility of AF ablation in an octogenerian patient.

Case report/ Case series	Indication	Preprocedural imaging	Guidance of ablation	Transseptal puncture	Ablation targets	Additional information
Kolakowski et al, 2023 (16)	Paroxysmal AF	TTE, CT scan	Fluoroscopy, TEE,	TSP into posterosuperior chamber (TEE-guided)	Single-shot cryoballoon PV isolation	Cryoablation in CTS, concomitant bicuspid aortic valve and CTS.
Lai et al, 2024 (17)	Persistent AF	TTE, TEE, CT scan	Fluoroscopy, ICE, 3D EAM	TSP into posterosuperior chamber (ICE-guided)	PV isolation, LA box lesion set, mitral isthmus line, vein of Marshall ethanol infusion, CTI line	Vein of Marshall ethanol infusion in patients with CTS.
Okuyama et al, 2024 (18)	Persistent AF	TTE, TEE, CT scan	Fluoroscopy, ICE, 3D EAM	TSP into posterosuperior chamber (ICE-guided)	PV isolation, SVC isolation, CTI line	/
Present case	Paroxysmal AF	TTE, TEE, MRI scan	Fluoroscopy, ICE, 3D EAM	TSP into posterosuperior chamber (ICE-guided)	Isolation of right PVs; isolation of left PVs could not be achieved	Additional separate membrane in front of left PV ostia verified by cardiac MRI and ICE.

AF – atrial fibrillation, TTE – transthoracic echocardiogram, TEE – transesophageal echocardiogram, TSP – transseptal puncture, EAM – electroanatomic mapping, CTS – cor triatritum sinister, PV – pulmonary vein, CT – computed tomography, ICE – intracardiac echocardiography, LA – left atrium, CTI – cavotricuspid isthmus, SVC – superior vena cava, AT – atrial tachycardia, MRI – magnetic resonance imaging

with PV ostia, and the anteroinferior section with mitral annulus and left atrial appendage. Contrary to the previous reports, the left PVs could not be mapped from the posterosuperior compartment of the LA, despite the use of a focal mapping and ablation catheter enabling point-by-point mapping to optimize maneuverability. Preprocedural MRI scan and ICE both revealed a separate thin membrane in front of the left PV ostia, which prevented catheter manipulation and access to the left PVs. Color Doppler on ICE revealed blood flow from the left PVs to the posterosuperior compartment, the left PVs were not dilated on the preprocedural MRI scan and there were no clinical signs of pulmonary congestion. Therefore, the blood flow into the posterosuperior compartment of the LA was not significantly obstructed. To the best of our knowledge, such a structure has not been reported previously in a case of catheter ablation in a patient with a CTS. Although only isolation of the right PVs could be performed, the patient has remained entirely asymptomatic for over 13 months. As the EAM of the left PVs could not be performed, their electrical activity could not be characterized. Consequently, the pathophysiological basis for the observed procedural success remains uncertain. Nevertheless, asymptomatic recurrence of AF cannot be excluded.

CONCLUSIONTS

Catheter ablation in patients with CTS and AF is a feasible and safe rhythm control treatment modality. However, comprehensive preprocedural anatomic characterization using complementary imaging modalities is essential given the altered atrial anatomy associated with CTS. An additional membranous structure, in front of the left PV ostia, may impede catheter access to the left PVs.

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