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The Final thesis

Differential Diagnosis of Secondary Hypertension: Literature Review and Clinical Case Analysis (title)

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SUMMARY

This thesis will delve into the complexities of accurately diagnosing secondary hypertension through a literature review and a detailed clinical case study. The clinical case centers on a 61-year-old male with significant cardiovascular and renal comorbidities, who struggled with persistent, treatment-resistant nocturnal hypertension. Traditional treatment methods were proven ineffective, prompting further, in-depth diagnostic exploration. The further diagnostic work-up led to the discovery and subsequent surgical excision of a large nasal polyp, which had been obstructing the patient's airway to the epiglottis. The excision led to a notable decrease in the patient's average systolic blood pressure by 20 mmHg.

This thesis delves into the complexities of diagnosing secondary hypertension, highlighting the critical role of atypical factors such as airway obstructions in its aetiology and management. It integrates insights from Rossi et al.'s "Practice Recommendations for Diagnosis and Treatment of the Most Common Forms of Secondary Hypertension" with findings from the NIH resource on the multifaceted causes and consequences of secondary hypertension. This synthesis emphasizes the global imperative for precise diagnosis and underscores persistent challenges in preventive strategies for cardiovascular health. Through this comprehensive examination, the thesis advocates for customized diagnostic approaches that enhance patient outcomes and contribute significantly to the evolution of personalized medicine, highlighting the essential nature of thorough diagnostic evaluations in managing complex cases of secondary hypertension.

KEYWORDS

Secondary hypertension, polymorbidity, airway obstruction, nasal polyp, cardiovascular disease, diagnostic strategies, personalized medicine.

INTRODUCTION

Hypertension, increasingly prevalent in the modern world, poses significant challenges for healthcare systems globally. As societies progress and lifestyles evolve, the incidence of hypertension, particularly secondary hypertension, is expected to rise. This form of hypertension, curable upon identification of its underlying causes, necessitates precise diagnostic and preventive strategies. Yet, despite the growing importance of accurate treatment and diagnosis, this task does not come easily, partly due to the absence of standardized diagnostic algorithms and effective prevention measures, complicating medical efforts. In this thesis, the focus will lie on why it is that there is no standardised algorithm for the diagnosis of the underlying conditions in secondary hypertension and why it is that prevention comes difficult.

Preventive strategies for secondary hypertension face significant challenges due to the complexity of its causes. The multicenter cross-sectional study "Secondary Cardiovascular Disease Prevention Deficit Persists over the Years" reveals ongoing gaps in effectively preventing secondary cardiovascular conditions, including hypertension. This study illustrates the difficulties in implementing targeted prevention measures that are adequately tailored to address specific aetiologies rather than broad, nonspecific lifestyle modifications. The findings indicate a need for enhanced screening and preventive practices that can detect and manage secondary hypertension early in its course.

The significance of this research is underscored by the findings of Rossi et al. and the multicenter study on secondary cardiovascular disease prevention. Rossi et al.'s practice recommendations provide a foundation for developing precise diagnostic algorithms that can significantly improve the management of secondary hypertension. Meanwhile, the documented persistent deficits in secondary cardiovascular disease prevention highlight the urgent need for improved preventive measures. Together, these studies demonstrate how advancements in both diagnosis and prevention could transform patient outcomes, reduce healthcare costs, and inform public health policies with a more nuanced approach to hypertension management.

CLINICAL CASE

Patient Profile

The patient came as a referral from "Diaverum Clinics" with the diagnosis of N18.5 Chronic kidney disease stage 5 for inpatient examination and treatment. A 61-year-old Caucasian male was seen with a significant history comprised of various cardiovascular and renal comorbidities. He presented with the main complaint of new, treatment resistant nocturnal hypertension along the last two months accompanied by constant general weakness, hoarseness, and drowsiness. During dialysis, his blood pressure reached about 220/110 mmHg.

Clinical Presentation

The patient presented with persistent, treatment-resistant nocturnal hypertension, with blood pressures reaching critically high levels during sleep. Traditional antihypertensive therapies had been ineffective, prompting a comprehensive re-evaluation of his condition.

Medical history

I10 Primary (essential) hypertension (acute and first-time diagnosed chronic disease)
Resistant arterial hypertension

Comorbid Diagnoses

I11.0 Hypertensive heart disease with heart failure (congestive) (chronic disease, first diagnosed this year)

- Hypertensive cardiopathy (left ventricular hypertrophy)
- CHF stage C with reduced EF, functional class III NYHA.

I25.2 Old myocardial infarction (other disease, rediagnosed 2024)

- Chronic coronary syndrome
- Acute myocardial infarction, type 2.
    - PCI and stenting (2002, 2006, 2010, 2021), PCI in-stent restenosis balloon angioplasty (2011, 2018)
    - PCI in-stent restenosis, PCI and stenting 3 DES (2021-02-09).

N18.5 Chronic kidney disease, stage 5 (chronic disease, first diagnosed 2024)

- Chronic kidney disease, stage G5D due to chronic glomerulonephritis (2004)

G47.32 Obstructive sleep apnoea syndrome (other disease, rediagnosed 2024)
E05 Thyrotoxicosis (hyperthyroidism)
J34.2 Deviated nasal septum
J33.0 Nasal polyp
J01.9 Acute sinusitis, unspecified

Life history and Progression of Disease

The patient experienced a substantial weight loss from 100 kg to 70.8 kg over the last six months (-29.2 kg).

Chronic Conditions and Treatments

2002, 2006, 2010 coronary stenting with additional percutaneous coronary intervention (PCI) due to coronary heart disease.
2004 Diagnosis of chronic glomerulonephritis, with subsequent progressive kidney damage.
2011 Increased serum creatinine levels
2016 Chronic kidney disease (CKD) stage 5 due to increased uremic factors
01/2018 Balloon angioplasty for in-stent stenosis.
07/2018 Regular dialysis thrice per week on odd days through AVF.
02/2021 Most recent PCI stent.

03/2021 Hospitalised in VULSK for acute myocardial infarction and treatments, followed by complications of unspecified bacterial infection and post-haemorrhagic anaemia.
09/2021 Managed at KMUK for coronary artery bypass grafting (AVJSO), shunting three coronaries.
09/2021 RITS due to postoperative pneumonia
10-11/2021 Rehabilitation in Kulautuva Rehabilitation Hospital
Suffers from gout and obstructive sleep apnoea, using a positive airway pressure device at night.
No significant cardiovascular pathology of other organ systems. No history of tuberculosis, jaundice, and no known allergies.

Family history

His son (deceased) also suffered from glomerulonephritis and had two kidney transplantations.

Medications

Table 1

Medication	Dosage	Regimen
Clopidogrel	75 mg	0-0-1
Losartan	100 mg	1-0-0
Moxonidine	0.4 mg	1-0-0.5
Doxazosin	8 mg	1-0-1
Aspirin	100 mg	0-0-1
Atorvastatin	40 mg	0-0-1
Isosorbide Mononitrate (Imdur)	60 mg	0-1-0
Olmesartan and Amlodipine (Sanoral)	20/5 mg	1-0-1
Allopurinol	100 mg	0-0-1
Thiamazole (Metizol)	5 mg	1-0-1
Tiapride	100 mg	1-0-0

Status upon entry: inconspicuous, haemorrhagic syndrome not present. Body surface area: 1.88 m² (height: 182 cm, weight:70.0 kg).

Diagnostic Work-up – Laboratory and instrumental investigations

Echocardiography March 10th, 2022

Structural and Functional Parameters (Table 2); increased left ventricular posterior wall diameter, moderately reduced ejection fraction.

Table 2

Parameter	Patient's value	Normal range
LVPWd (Left ventricular posterior wall diameter, diastolic)	54.5 mm	5.3 mm – 5.9 mm
IVSd (Intraventricular septum diameter, diastolic)	12 mm	0.9 mm – 1.0 mm
LVIDd (Left ventricular internal diameter, diastolic	11 mm	0.9 mm – 1.0 mm
EF (Ejection Fraction)	45 %	55 – 70 %
LVIDs (Left ventricular internal diameter, systolic)	38 mm	Approx. 2.7 mm
LVPWs (Left ventricular posterior wall diameter, systolic)	50.4 mm	5.3 mm – 5.9 mm
LVOT (Left ventricular outflow tract)	51 mm	20-37 mm
Aortic Ring Diameter	23 mm	20 – 40 mm
Aortic Sinus Diameter	37.5 mm	34 – 40 mm
Ascending Aorta Diameter	3.7 mm	25 – 37 mm

Doppler and flow parameters (Table 3); normal filling pressure, but increased deceleration time suggestive of diastolic dysfunction.

Table 3

Parameter	Patient's value	Normal range
E (early diastolic filling) wave velocity	1.04 m/s	0.6 – 1.3 m/s
A (atrial contraction) wave velocity	1.26 m/s	0.4 – 1.0 m/s
E/A ratio	1	1-2
Deceleration time (DT)	356 ms	150 – 240 ms

Valve pathology and additional findings (Table 4); indicative of aortic valve insufficiency, additional pathological findings are listed in the table.

Table 4

Parameter	Patient's value	Normal range
Aortic Valve Velocity (Vmax)	2.2 m/s	1 – 1.7 m/s

Mitral valve regurgitation	Grade I	
Tricuspid valve regurgitation	Grade I	
Ascending Aorta	Not dilated, calcinoid, sclerotic	
Right heart chambers	Increased in size	
Left ventricular (LV) hypertrophy	Concentric type	
LV systolic function	Moderately reduced due to hypokinesia of the LVPW	
LV diastolic function	Impaired relaxation, indicative of early-stage diastolic dysfunction	
Pulmonary artery (PA) acceleration time	Normal, non-hypertensive PA circulation curve	

Blood pressure measurement March 22nd, 2022: SBP 219 mmHg / DBP 99 mmHg

Examinations in "Diaverum Clinics" (Table 5), March 23rd, 2022:

Table 5

Parameter	Patient's value	Normal range
Hb (Haemoglobin)	121 g/L	135 – 175 g/L
Ht (Haematocrit)	34.5 %	40 – 52 %
P (Phosphorus)	2.12 mmol/L	0.81 – 1.45 mmol/L
Ca (Calcium)	2.49 mmol/L	2.20 – 2.60 mmol/L
K (Potassium)	4.27 mmol/L	3.5 – 5.1 mmol/L
Urea	16.4 mmol/L	2.5 – 7.1 mmol/L
Creatinine	922 µmol/L	60 – 110 µmol/L
Ferritin	268.3 µg/L	30 – 400 µg/L
PTH (Parathyroid hormone)	15.2 pmol/L	1.6 – 6.9 pmol/L
CRP (C-reactive protein)	1.65 mg/L	< 5 mg/L

Examination in Dialysis Department (Table 6), March 25th, 2022:

Table 6

Parameter	Patient's value	Normal range
Urea	17.2 mmol/L	2.5 – 7.1 mmol/L
Creatinine	883 µmol/L	60-110 µmol/L
eGFR (CKD-EPI)	<15 mL/min/1.73m²	>90 mL/min/1.73m²
CRP	26.1 mg/L	<5 mg/L
K	5.9 mmol/L	3.5 – 5.1 mmol/L
Iron (Fe)	77 µmol/L	11 – 30 µmol/L

Phosphorus	1.71 mmol/L	0.81 – 1.45 mmol/L
LYM (Lymphocytes)	0.50 x10^9/L	1.2 – 3.4 x10^9/L
RBC (Red blood cells)	4.06 x10^12/L	4.5 – 5.9 x10^12/L
Hb	125 g/L	135 – 175 g/L

Infectious diseases laboratory, sample/Specimen Nasal swab, March 28th, 2022:
Culture test (Diagnosis of COVID-19 caused by SARS-COV-2 virus): Not detected.
Repeated on April 12th, also Not detected.

24-Hour Blood Pressure (BP) Monitoring and circadian rhythm plot, March 29th-30th, 2022:
This examination revealed elevated systolic blood pressures (SBP) with peaks at 216 mmHg and diastolic blood pressures (DBP) up to 120 mmHg. Notably, the systolic blood pressure frequently exceeded the upper normal limit of 140 mmHg, with the highest readings occurring at night, indicative of significant nocturnal hypertension. The full 24-hour BP monitoring is shown in *Figure 1*. To conclude the blood pressure changes to be nocturnal or dependent of the circadian rhythm, a circadian rhythm plot was conducted. The graph can be seen in *Figure 2*.

The graph shows that the mean systolic blood pressure (SBP) over 24 hours was recorded at 176.9 mmHg, and the diastolic blood pressure (DBP) at 98.3 mmHg, significantly above normal values. The amplitude of variation for SBP was 17.0 mmHg and for DBP 8.6 mmHg, indicating pronounced diurnal fluctuations which are physiologically expected but were notably heightened in this hypertensive state [1].

The pulse data revealed a percent rhythm of 0.646, illustrating a strong circadian influence on heart rate fluctuations. Moreover, the nocturnal acrophase for both SBP and DBP around midnight is slightly atypical as blood pressure typically dips during the night in a normal circadian pattern ("dipping"). The observed pattern indicates a "non-dipping" or "reverse dipping" trend, which has been associated with a higher cardiovascular risk [2].

This comprehensive analysis underscores the importance of considering circadian factors in managing hypertension. Tailoring treatment strategies to align with the individual's biological rhythms could optimize blood pressure control and reduce cardiovascular risk [3]. Given the documented "non-dipping" or "reverse dipping" patterns and the associated increased cardiovascular risk, a holistic approach involving a re-evaluation of the current management plan and an exploration of secondary causes of hypertension, as was conducted, is crucial [4].

Figure 1: 24- hour blood pressure monitoring.

Measurement time :29-03-2022 12:00 -> 30-03-2022 15:00
Printout :30-03-2022

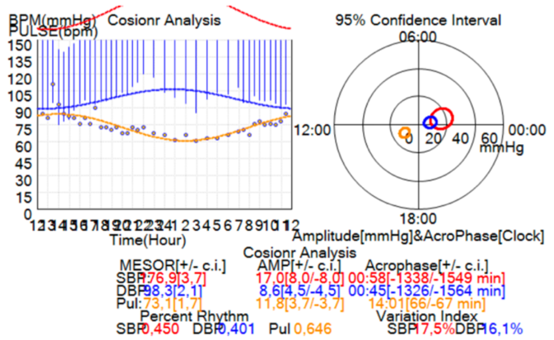
BP DATA

No.	DATE	TIME	SYS	DIA	MAP	PUL	DP	STATUS	Comment
1	29-03-2022	12:30	169	89	115	85	14,3	0 - --	
2	29-03-2022	13:00	163	89	113	81	13,2	0 - --	
3	29-03-2022	13:30	170	95	120	111	18,8	0 - --	
4	29-03-2022	14:00	142	75	97	93	13,2	0 - --	
5	29-03-2022	14:30	140	78	98	85	11,9	0 - --	
6	29-03-2022	15:00	144	80	101	83	11,9	0 - --	
7	29-03-2022	15:30	147	88	107	81	11,9	0 - --	
8	29-03-2022	16:00	150	94	112	76	11,4	0 - --	
9	29-03-2022	16:30	177	97	123	81	14,3	0 - --	
10	29-03-2022	17:00	180	95	123	76	13,6	0 - --	
11	29-03-2022	17:30	169	93	118	90	15,2	0 - --	
12	29-03-2022	18:00	169	98	121	73	12,3	0 - --	
13	29-03-2022	18:30	161	96	117	73	11,7	0 - --	
14	29-03-2022	19:00	173	99	123	71	12,2	0 - --	
15	29-03-2022	19:30	178	99	125	73	12,9	0 - --	
16	29-03-2022	20:00	195	104	134	68	13,2	0 - --	
17	29-03-2022	20:30	199	102	134	68	13,5	0 - --	
18	29-03-2022	21:00	206	109	141	73	15,0	0 - --	
19	29-03-2022	21:30	199	113	141	71	14,1	0 - --	
20	29-03-2022	22:00	216	120	152	73	15,7	0 - --	
21	29-03-2022	23:00	177	117	137	68	12,0	0 - --	
22	30-03-2022	00:00	172	104	126	66	11,3	0 - --	
23	30-03-2022	01:00	186	99	128	62	11,5	0 - --	
24	30-03-2022	02:01	196	94	128	66	12,9	0 - --	
25	30-03-2022	03:00	171	86	114	61	10,4	0 - --	
26	30-03-2022	04:00	182	98	126	63	11,4	0 - --	
27	30-03-2022	05:00	189	104	132	63	11,9	0 - --	
28	30-03-2022	06:00	183	102	129	66	12,0	0 - --	
29	30-03-2022	07:00	190	108	135	69	13,1	0 - --	
30	30-03-2022	07:30	170	95	120	71	12,0	0 - --	
31	30-03-2022	08:00	170	96	120	66	11,2	0 - --	
32	30-03-2022	08:30	179	101	127	76	13,6	0 - --	
33	30-03-2022	09:00	165	97	119	78	12,8	0 - --	
34	30-03-2022	09:30	165	96	119	75	12,3	0 - --	
35	30-03-2022	10:00	157	97	117	76	11,9	0 - --	
36	30-03-2022	10:30	168	94	118	75	12,6	0 - --	
37	30-03-2022	11:00	173	91	118	78	13,4	0 - --	
38	30-03-2022	11:30	172	93	119	85	14,6	0 - --	
39	30-03-2022	12:00	178	95	122	85	15,1	0 - --	
40	30-03-2022	12:30	150	89	109	90	13,5	0 - --	
41	30-03-2022	13:00	146	87	106	73	10,6	0 - --	
42	30-03-2022	13:30	---	---	---	---	---	*0 E 10	Large motion error
43	30-03-2022	14:00	163	99	120	83	13,5	0 - --	

Figure 2: Circadian rhythm plot.

Patient ID. [redacted]
Patient Name [redacted]
Measurement time :29-03-2022 12:00 -> 30-03-2022 15:00
Printout :30-03-2022

Circadian Rhythm Plot



<u>Biochemistry (Table 7)</u>, March 30th, 2022:

Table 7

Parameter	Patient's value	Normal range

BNP	839.4	< 100 ng/L
CRP	53.9	< 5 mg/L
TSH (Thyrotropin)	0.016	0.4 – 4.0 mU/L
FT4 (Free Thyroxine)	19.50	12 – 22 pmol/L
T3 (Triiodothyronine)	0.91	1.3 – 3.1 nmol/L
PSA (prostate-specific antigen)	5.963	0.0 – 4.0 µg/L

In the clinical case analysis, it is invaluable to delineate the intricate pathophysiological interactions among the diagnosed conditions with exacting medical precision. The patient suffers from End-Stage Renal Disease (ESRD), indicated by persistently elevated urea levels of 16.4 mmol/L and 17.2 mmol/L, and creatinine concentrations initially at 922 µmol/L, subsequently reducing to 883 µmol/L (see *Table 6* and *Table 5*). The critically low glomerular filtration rate (eGFR) below 15 mL/min/1.73 m² places the renal impairment as stage 5 chronic kidney disease (CKD), necessitating routine dialysis intervention, as is already known to the patient since 2018. Additionally, elevated serum levels of natriuretic peptides such as BNP are known to increase in cases of reduced renal and liver function, as both organs are likely involved in their metabolism. This increase could be attributed to the delayed breakdown of these peptides due to the organ dysfunction, further highlighting the patient's impaired renal function, as is seen in the BNP value of 839.4 ng/L (see *Table 7*) [5]. This may also indicate hypervolemia with fluid overload and subsequent heart failure. Therefore, higher ultrafiltration volume was tried to achieve during dialysis sessions, without much influence on the patient's high blood pressure.

Concurrently, the patient's cardiovascular profile is dominated by severe hypertensive heart disease, evidenced by peak systolic blood pressures of 216 mmHg and echocardiographic indicators of left ventricular hypertrophy coupled with a compromised ejection fraction (EF) of 45%. These findings are pathognomonic of congestive heart failure (CHF) Stage C, characterized by significantly reduced cardiac output leading to symptomatic heart failure. Additionally, the presence of hyperthyroidism adds a layer of complexity, influencing systemic metabolic rate and cardiovascular dynamics, which could exacerbate cardiac symptomatology [6]. This case mandates a comprehensive, multidisciplinary management approach that encompasses nephrological therapy, cardiovascular intervention, and endocrine regulation to optimize therapeutic outcomes and decelerate disease progression.

Detailed Analysis of Multidisciplinary Management in Secondary Hypertension

The management of secondary hypertension in this 61-year-old male patient exemplifies the critical need for a multidisciplinary approach, given the complex interplay of cardiovascular, endocrine, and respiratory factors influencing his condition. Specific consultations and interventions that highlight the pathophysiological intricacies and tailored management strategies employed were the following:

Cardiovascular Dynamics and Management

As mentioned, on March 30, 2022, cardiovascular assessment revealed exceptionally high systolic blood pressures, peaking at 216 mmHg, reflecting the severity of his hypertensive state, which necessitated meticulous adjustments during his haemodialysis sessions to manage chronic fluid overload effectively. Haemodialysis sessions were closely monitored, with specific adjustments in ultrafiltration volumes to mitigate hypertensive episodes—reflecting an essential component in the management of fluid dynamics in hypertensive patients with renal failure.

Further compounding the cardiovascular challenge were the echocardiographic findings from March 10, 2022, which demonstrated significant left ventricular hypertrophy with an ejection fraction reduced to 45% (see *Table 2*, *Table 3*, *Table 4*). These findings are indicative of advanced hypertensive heart disease and congestive heart failure (CHF) Stage C, necessitating comprehensive cardiovascular management that includes rigorous monitoring and potential consideration for renal denervation to address resistant hypertension.

Endocrine Considerations and Thyrotoxicosis Management:

The endocrine system's role in this clinical scenario is of importance, considering that thyrotoxicosis can significantly influence the patient’s cardiovascular health. On March 31, 2022, endocrine assessment confirmed the presence of hyperthyroidism (see *Table 8*), necessitating rigorous management with methimazole. Hyperthyroidism is known to increase heart rate, enhance cardiac contractility, and reduce systemic vascular resistance, collectively escalating cardiac output which can exacerbate existing heart conditions. Methimazole functions by inhibiting the synthesis of thyroid hormones, thus alleviating these hypermetabolic effects. The strategic control of thyroid hormone levels is crucial not only for reducing cardiac stress but also for stabilizing hemodynamic parameters, essential in patients undergoing hemodialysis where fluid balance and cardiovascular stability are already compromised and could be further complicated by hyperthyroidism [7].

Table 8

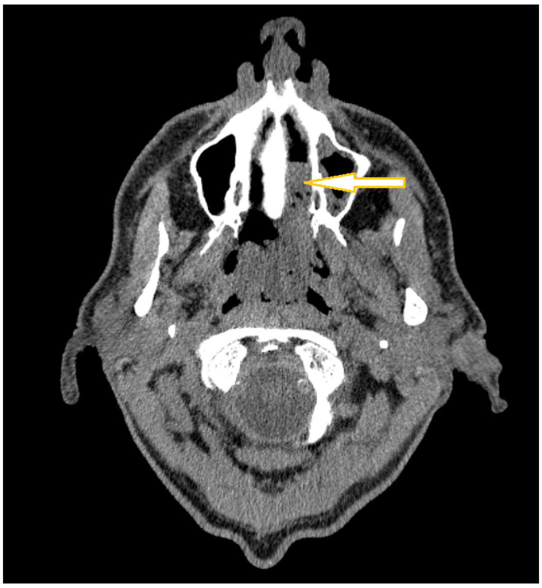
Parameter	Patient’s value	Normal range
TSH (Thyroid-Stimulating Hormone)	0.016 mU/L	0.4 – 4.0 mU/L

FT4 (Free Thyroxine)	19.50 pmol/L	12 – 22 pmol/L
T3 (Triiodothyronine)	0.91 nmol/L	1.3 – 3.1 nmol/L

Respiratory and Otorhinolaryngological (ENT) Management

The ENT management became a focal point following the discovery and removal of a large nasal polyp on April 7, 2022. This surgical intervention was critical as the polyp was implicated in causing obstructive sleep apnoea, which in turn was exacerbating the patient's nocturnal hypertension—characterized by non-dipping blood pressure patterns during sleep. Obstructive sleep apnoea is known to induce nocturnal hypoxemia and hypercapnia, which can trigger sympathetic nervous system activation, leading to increased nocturnal blood pressure. The successful removal of the obstruction thus led to a marked improvement in sleep quality and respiratory efficiency, contributing significantly to better blood pressure management. This highlights the interlinked nature of airway integrity and cardiovascular health and accentuates the importance of a thorough ENT evaluation in patients with secondary hypertension, where airway obstructions might contribute to complex hypertensive profiles [8].

Figure 3: Nasal polyp. Axial CT scan of the nasopharynx, showing a well-defined, hypodense lesion of the nasopharynx protruding into the oropharyngeal region. Due to its smooth contour and homogenous density, this is most likely a nasal polyp. Right septum appears deviated. Adjacent sinuses and the oropharyngeal airway remain clear and without signs of secondary sinusitis or other pathologic findings.



Comprehensive Integration of Multidisciplinary Findings

This patient's case exemplifies the intricacies of managing secondary hypertension with multiple interlinked comorbid conditions. Each specialty's insights – cardiovascular, endocrine, and respiratory – contribute to a holistic understanding of the patient's health challenges. The integration of these findings into a unified management strategy emphasises the necessity of a multidisciplinary approach. The dynamic and tailored treatment adjustments, in response to ongoing assessments, highlight the critical need for continual monitoring and adaptation of therapeutic strategies. The effective management of this case rests on understanding the profound pathophysiological interactions between renal and systemic vascular resistance, thyroid dysfunction, and airway obstructions, all of which play a significant role in the modulation of blood pressure and overall disease progression [9].

Pathophysiological interconnection

Thyroid function and cardiovascular health:

Cardiac function: Thyroid hormones (TH) have profound effects on the cardiovascular system. Thriiodothyronine (T3), which is the active form of TH, increases the heart rate, cardiac contractility, and cardiac output by upregulating the expression of myocardial calcium ATPase and ß-andrenergic receptors, hereby enhancing both the sensitivity and the responsiveness of the heart to the catecholamine hormones. Any excess to the thyroid hormones can lead to tachycardia, an increased LV ejection fraction, and sometimes even to cardiomyopathy. Yet prolonged exposure to high levels of thyroid hormones, such as in cases of hyperthyroidism, can lead to desensitization of β-adrenergic receptors, and may also influence the turnover rate of those receptors, affecting their availability for catecholamine binding. Changes in receptor recycling and degradation processes can contribute to alterations in receptor sensitivity over time [10]. In the case presented, echocardiographic assessments on March 10, 2022, revealed left ventricular hypertrophy and a reduced ejection fraction (EF) of 45%. These findings are clinically significant and can be directly linked to the patient's thyrotoxic state. Thyroid hormones, particularly triiodothyronine (T3), enhance myocardial contractility and increase heart rate, which can initially lead to an increased ejection fraction. However, in chronic conditions like ours, where prolonged exposure to high thyroid hormone levels persists, there is a potential for cardiac hypertrophy and subsequent cardiac dysfunction, culminating in a decreased ejection fraction. This progression aligns with the mechanisms of thyroid hormone-induced changes in myocardial energy demands and oxidative stress, which, over time, can lead to structural and functional cardiac alterations.
Vascular effects: Hyperthyroidism is associated with a decrease in systemic vascular resistance due to the relaxation of vascular smooth muscle in the tunica media of the vessels throughout the body. Thyroid hormones can also enhance the production of nitric oxide (NO), a potent vasodilator, which works by diffusing into the underlying vascular smooth muscle cells, causing relaxation and subsequent vasodilation. Intracellular calcium decrease can also

lead to smooth muscle cell relaxation and vasodilation, as calcium can be affected by thyroid hormones via the modulation of ion channel activity in vascular smooth muscle cells, including calcium channels, where this works by reducing calcium influx into smooth muscle cells, thereby attenuating vasoconstriction and counteracting vasoconstrictor substances like norepinephrin, angiotensin II and endothelin-1, which would typically increase intracellular calcium levels, leading to smooth muscle contraction and vasoconstriction [11].

<u>Airway integrity and cardiovascular health:</u>
Obstructive sleep apnoea (OSA) and hypertension: OSA is characterised by repeated episodes of partial or complete obstruction of the upper airway during sleep, which leads to intermittend hypoxia, increased sympathetic activity, and namely to “non-dipping” hypertension. The repetitive oxygen desaturations and subsequent reoxeginations cause oxidative stress, systemic inflammation, and are associated with endothelial dysfunction, predisposing affected individuals to atherosclerosis, further exacerbated hypertension, coronary artery disease, and stroke [12].
Mechanical impact of airway obstructions: Mechanical obstructions, as in this case a nasal polyp, can further contribute to the development of OSA, by increasing the resistance to airflow, causing the need for higher effort to breathe, and intensifying negative thoraxic pressures. The negative intrathoracic pressure generated during obstructive respiratory efforts increases left ventricular transmural pressure (the pressure gradient across the ventricular wall), thereby increasing cardiac workload and myocardial oxygen demand. Over time, these recurrent episodes contribute to the development of left ventricular hypertrophy, as observed in the echocardiographic findings of March 10, 2022, where left ventricular hypertrophy was noted along with a decreased ejection fraction.

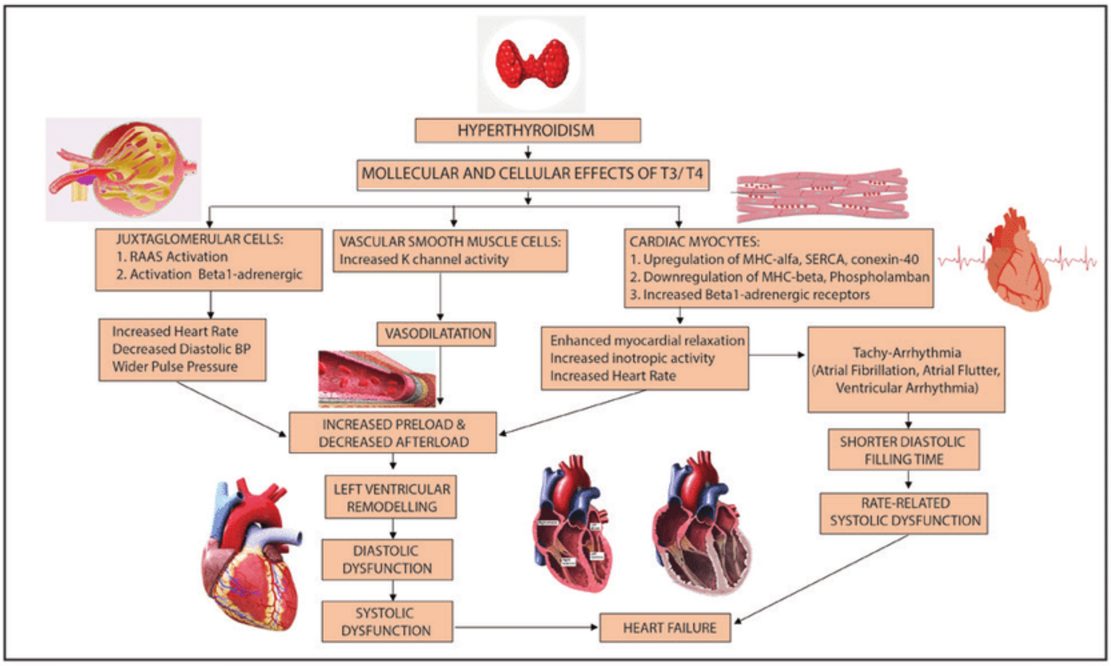
<u>Interplay between thyroid function and airway integrity</u>
Metabolic and respiratory demands: Thyrotoxicosis increases the metabolic rate by stimulating the expression of enzymes involved in glycolysis, the tricarboxylic acid (TCA) cycle, and oxidative phosphorylation in the mitochondria, enhancing cellular energy production. This increased mitochondrial activity and ATP synthesis result in an elevated basal metabolic rate (BMR). Furthermore, this increase in metabolic rate driven by thyroid hormones results in greater cellular energy production, which necessitates higher oxygen consumption to fuel oxidative phosphorylation in the mitochondria. This increased oxygen demand is particularly pronounced in tissues of high metabolic activity, such as the heart, skeletal muscles, liver, and brain, which rely heavily on aerobic metabolism for energy

production. In the context of thyrotoxicosis, OSA and the mechanical obstruction, all this can lead to a worsening of the hypoxemia, subsequently causing even higher hypertension and exacerbating our patient's clinical picture. The increased metabolic rate also causes an increased cardiac output, to ensure adequate oxygen delivery and tissue perfusion in order to meet the heightened metabolic needs of the body. Increased metabolic demands can also lead to sympathetic nervous system activation, which exerts a positive chronotropic and inotropic activity [13]. The increased cardiac output can also be explained by the Frank-Sterlin Mechanism: This mechanism describes the relationship between preload and stroke volume. Increased metabolic demands may lead to an increase in venous return, thereby increasing preload and subsequently enhancing stroke volume and cardiac output.

Inflammatory and immunological apsects: The pathophysiology of the inflammatory interaction between thyroid disorders, such as thyrotoxicosis, and chronic airway diseases involves several interconnected mechanisms. Thyroid disorders, including thyrotoxicosis, are associated with dysregulation of the immune system, leading to altered immune responses and increased production of pro-inflammatory cytokines. Chronic airway diseases, for example, asthma and chronic obstructive pulmonary disease (COPD), also involve immune-mediated inflammatory processes within the airways. The dysregulated immune responses in both thyroid disorders and chronic airway diseases can contribute to the persistence of inflammation and exacerbation of airway pathology. Inflammatory cells, such as macrophages, lymphocytes, and eosinophils, release various cytokines, chemokines, and inflammatory mediators in response to immune activation. Thyrotoxicosis is associated with increased production of cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), which express pro-inflammatory effects and can contribute to further airway inflammation, which is characterized by infiltration of inflammatory cells, mucosal edema, as well as increased mucus production. This inflammation can be exacerbated due to thyrotoxicosis by amplified immune responses and cytokine production, leading to increased airway swelling and obstruction [14]. Prolonged inflammation in the airways can lead to airway remodeling, characterized by thickening of the airway walls, increased smooth muscle mass, and fibrosis. This can exacerbate respiratory symptoms such as dyspnoea, wheezing, coughing, and chest tightness, and lead to a decrease in respiratory function and increased morbidity.

A simple visualisation of the thyroid hormones‘ effects can be seen in *Figure 4*.

Figure 4: Effects of thyroid hormones on cardiovascular hemodynamic and its progression to heart failure [15].



Detailed analysis of the pharmacological antihypertensive management

The management of secondary hypertension, particularly in patients presenting with multiple comorbidities and a history of treatment resistance, demands a tailored pharmacological approach, targeting various pathophysiological mechanisms. A clear understanding of the molecular mechanisms and hence a proper therapeutic rationale for each drug utilised in the treatment regimen is essential. A complete list of the patient's medication regimen can be seen in *Table 1*. Despite the patient's rigorous medication regimen, persistent elevation in blood pressure highlighted the multifactorial aetiology of secondary hypertension. This includes the complex interaction between cardiovascular pathology, renal dysfunction, and endocrine disturbances such as hyperthyroidism, which exacerbated systemic hypertension.

<u>Losartan</u>

The patient takes 100 mg of Losartan daily. Losartan is a selective antagonist of angiotensin II type 1 (AT1) receptors and a key player in the renin-angiotensin-aldosterone (RAAS) system. Angiotensin II is the principal effector molecule of the RAAS and exerts significant effects on renal physiology, mainly via the AT1 receptor. By blocking with the AT1 receptors, angiotensin II promotes vasoconstriction, aldosterone secretion, sodium retention and potentiation of sympathetic nervous system activity, which all contributes to increased blood pressure and renal stress. By being an antagonist to the AT1 receptors, Losartan leads to a reduction in the efferent arteriolar tone compared to the afferent arteriole inside the glomerulus. This differential action decreases intraglomerular hypertension and lowers glomerular capillary hydraulic pressure, thereby mitigating the transcapillary driving force for protein filtration and commensurately proteinuria. Proteinuria exacerbates kidney damage through inflammatory and fibrotic pathways, and its reduction is an essential target in the management of renal disease in hypertensive patients [16]. Another effect Losartan exhibits by blocking AT1 receptors is the reduction of the secretion of the mineralocorticoid aldosterone from the adrenal cortex. As a mineralocorticoid, aldosterone enhances sodium and water resorption in the renal tubules, leading to an increase in intravasal volume and blood pressure. Aldosterone has also been implicated in direct kidney damage by promoting fibrosis. Losartan has been demonstrated to attenuate the expression of transforming growth factor-beta (TGF-β) and the deposition of extracellular matrix proteins in the kidney, thereby interrupting this fibrotic pathway, aiding in the preservation of renal architecture and function [17]. Therefore, by reducing aldosterone levels and TGF- β expression, Losartan aids in decreasing the volume overload and fibrotic remodelling of renal tissue. The combined antihypertensive and nephroprotective qualities make Losartan an efficient agent in the patient's pharmacological therapy.

Moxonidine

The patient takes 0.4 mg in the morning and 0.2 mg in the evening. Moxonidine is a selective agonist for imidazoline receptor subtype 1 (I1) in the rostral ventrolateral medulla, a critical centre for cardiovascular regulation. Activation of these receptors has a direct inhibitory effect on the central sympathetic nervous system, which is hyperactive in conditions like hypertension and chronic kidney disease (CKD). Moxonidine's action at the I1 receptor induces a decrease in the generation and propagation of sympathetic nervous impulses, thereby lowering the catecholamine release from the sympathetic nerve terminals. Through this, a decreased stimulation of α- and β-adrenergic receptors in the heart and vasculature is achieved, resulting in reduced heart rate (chronotropic effect) and myocardial contractility (inotropic effect), as well as vasodilation. The net effect is a significant reduction in arterial pressure. The reduction in sympathetic drive is also of particular importance for renal function in hypertensive patients, as elevated sympathetic activity contributes to increased renal vascular resistance, which can impair renal blood flow. Moxonidine alleviates this condition by decreasing renal vascular resistance, enhancing renal perfusion. Improved blood flow to the kidneys helps in maintaining glomerular filtration rate (GFR) and facilitates the excretion of sodium and water, further aiding in blood pressure control [18]. Beyond its primary cardiovascular effects, Moxonidine also offers potential neuroprotective benefits due to its central action: Through modulation of the central sympathetic tone, it may reduce the stress-related neurohormonal activation. In the kidneys, reduced sympathetic activity helps to prevent pathologic changes associated with CKD, such as glomerulosclerosis and interstitial fibrosis. Particularly in patients with CKD, the reduction of systemic blood pressure and improvement in renal hemodynamic are crucial for slowing the progression of renal disease. Moxonidine, by targeting the central mechanisms of hypertension, offers the dual benefit of effective blood pressure reduction and protective effect on renal function. Moxonidine's unique action on imidazoline receptors in the RVLM makes it a crucial component of the therapeutic regimen in this hypertensive patient, especially with his concomitant chronic kidney disease, offering both cardiovascular and nephroprotective advantages together with Losartan's.

Doxazosin

4 mg twice are taken daily of this Alpha-1 Adrenergic receptor antagonist in vascular smooth muscle. The blockage of these receptors causes vasodilation, both arterial and venous. Arterial vasodilation leads to a decrease in systemic vascular resistance, directly lowering arterial blood pressure. Venous dilation reduces venous return to the heart, decreasing the cardiac preload. This reduction is particularly beneficial in patients with congestive heart failure (CHF), as Doxazosin effectively reduces the cardiac workload, hence decreasing the heart's oxygen demand. This is an essential requirement to prevent myocardial ischemia in patients with CHF, as the myocardium's adequate oxygenation is endangered by coronary artery disease or myocardial damage [19]. In conclusion, Doxazosin's ability to block alpha-1 adrenergic receptors results in a comprehensive cardiovascular effect—reducing arterial pressure, easing the cardiac workload, and enhancing the overall efficiency of the heart. These pharmacodynamic properties render it an essential component of hypertension management, especially in patients with coexisting congestive heart failure.

Amlodipine

The daily intake of the calcium channel blocker combination of Olmesartan and Amlodipine is 20/5 mg. Amlodipine belongs to the dihydropyridine class of calcium channel blockers and selectively inhibits the influx of calcium ions through L-type calcium channels in the cardiac and vascular smooth muscle, leading to vasodilation primarily in the peripheral arterioles. By reducing the force of cardiac contraction and arterial pressure, amlodipine significantly lowers the workload, myocardial oxygen consumption, the afterload and systemic blood pressure. Although Amlodipine is primarily used for hypertension and angina, the reduction in arterial pressure and cardiac demand can also indirectly benefit patients with heart failure, as it eases the overall functional demands placed on the heart. Its role in reducing peripheral resistance and myocardial workload, while enhancing coronary perfusion, underscores its utility in a broad spectrum of cardiovascular pathologies [20].

Isosorbide Mononitrate (IM)

60 mg are taken of this. IM provides dilation of veins and arteries and facilitates the release of nitric oxide (NO) inside the vascular smooth muscle. The release of NO activates guanylate cyclase, which in turn increases cyclic guanosine monophosphate (cGMP) and leads to smooth muscle relaxation. IM's ability to induce both venous and arterial dilation significantly reduces the preload and afterload and helps in managing symptoms of heart failure and angina by decreasing myocardial oxygen demand [21].

Captopril

50 mg can be taken as needed of this Angiotensin-Converting Enzyme (ACE) inhibitor. As Captopril inhibits the enzyme responsible for converting angiotensin I to angiotensin II, it lowers the levels of angiotensin II, which leads to decreased vasopressor activity and reduced aldosterone secretion. The decrease in vasopressor activity leads to vasodilation and a reduction in blood volume, enabling better control of high blood pressure [22]. By reducing aldosterone secretion, Captopril exerts similar nephroprotective qualities as Losartan, as the reduced secretion helps in controlling the progression of renal disease by decreasing the intraglomerular pressure and mitigating proteinuria.

DISCUSSION

Secondary hypertension (SH) represents a subset of hypertension characterized by an identifiable, often not only treatable, but altogether preventable cause. Despite its significant clinical implications, SH remains underdiagnosed, potentially leading to suboptimal patient outcomes. To delve deeper into the complex aetiology of secondary hypertension, a nuanced comparative analysis of two seminal articles is proposed. This examination will illuminate the diverse mechanisms and clinical implications that underly this condition, emphasizing on the interplay between cardiovascular, renal, and endocrine factors that complicate its management. Such a scholarly comparison not only enriches our understanding but also guides the refinement of therapeutic strategies tailored to the multifactorial nature of secondary hypertension. The articles we will discover are Hegde et al.'s "Secondary Hypertension", a comprehensive review on the disease and Rossi et al.'s "Practice Recommendations for Diagnosis and Treatment of the Most Common Forms of Secondary Hypertension", which offers focused guidelines on diagnosis and management. The literature search was strategically conducted using comprehensive databases such as PubMed and Embase, focusing on high-level evidence including randomized controlled trials, meta-analyses, and systematic reviews. The search utilized keywords specifically related to secondary hypertension and its diverse aetiologies, ensuring a broad yet relevant collection of data to support this thesis. In addition to the article, we will be integrating insights from our unique clinical case involving the nasal polypus. These resources collectively emphasize the complexity and diverse aetiology of secondary hypertension, advocating for more meticulous diagnostic processes and personalized treatment strategies. The nuanced understanding of SH provided by Rossi et al. in their comprehensive review of diagnosis and treatment practices, alongside Hedge et al.'s exploration of its genetic and molecular dimensions, offers a robust framework for addressing this critical healthcare challenge.

Hegde et al.'s extensive overview serves as a foundational resource in understanding the broad spectrum of conditions that can precipitate secondary hypertension and can be seen as a guideline for everyday practice. The article thoroughly outlines various causes such as renal dysfunction, endocrine abnormalities, and vascular irregularities, each associated with distinct but interconnected pathophysiological mechanisms. This broad and comprehensive perspective is essential for medical professionals to not only appreciate the potential complexities involved in diagnosing and managing secondary hypertension but to understand their relation to each other and to develop a gut-feeling for when to suspect the diagnosis and how to investigate it.

Rossi et al. emphasize a systematic approach to the diagnosis of SH, advocating for a thorough evaluation in patients presenting with signs suggestive of secondary causes. This includes young patients with severe or resistant hypertension, those with abrupt onset of hypertension, and patients with incidental findings that suggest endocrinopathies or renovascular disease. Their approach underscores the importance of a comprehensive patient history, physical examination, and the strategic use of diagnostic tests to uncover the root causes of SH, such as renal artery stenosis or hormonal excess.

Conversely, Hedge et al. provide a detailed examination of the genetic underpinnings of SH, discussing how specific mutations and genetic predispositions contribute to the development of conditions like primary aldosteronism and pheochromocytoma. Their work suggests that understanding these genetic factors can significantly enhance the precision of both diagnosis and treatment, enabling personalized medicine approaches that target the molecular basis of the disease.

Rossi et al. provide a narrower lens, concentrating specifically on the most prevalent forms of secondary hypertension encountered in clinical practice. Their highly pragmatic approach offers detailed diagnostic algorithms and treatment protocols. These recommendations are designed to guide clinicians through the intricate decision-making process required to pinpoint the underlying causes of hypertension and tailor interventions accordingly. The specificity of Rossi et al.’s guidelines aids in the practical application of complex clinical data, facilitating more targeted and effective management strategies.

The clinical case presented in this thesis adds a novel dimension to the discourse on secondary hypertension. It involves a patient whose uncontrolled hypertension, characterized by nocturnal rises in arterial blood pressure, was ameliorated following the surgical removal of a substantial nasal polypus. This intervention led to a notable decrease in the patient's average systolic ABP by 20 mmHg. The rarity of this case highlights an often-overlooked cause of secondary hypertension linked to Ear, Nose, Throat (ENT) disorders. Such cases underscore the need for clinicians to maintain a high index of suspicion for less typical aetiologies, especially when conventional causes have been excluded and hypertension remains uncontrolled.

The juxtaposition of the clinical case against the backdrop of the literature not only bridges the gap between theory and practice but also illuminates areas where current research may be lacking. The substantial improvement in hypertension management following an intervention for an uncommon cause suggests potential areas for further inquiry. Specifically, the underrepresentation of ENT-related obstructions within the broader discussions on secondary hypertension points to a need for increased awareness and research into how these conditions can impact cardiovascular health.

Moreover, the success observed in the clinical case following the polypectomy supports Rossi et al.’s emphasis on cause-specific interventions. It also prompts a re-evaluation of diagnostic workflows and treatment paradigms to incorporate a wider range of potential aetiologies, including those within the ENT spectrum. This approach could lead to significant improvements in patient outcomes, particularly in cases where traditional pathways of investigation fail to yield conclusive results. It is important to note that the application of this research could vary significantly by region, reflecting diverse healthcare system capabilities and the prevalence of secondary hypertension. For instance, regions with limited access to advanced diagnostic tools might focus on implementing basic screening protocols and community awareness programs. In adapting the diagnostic frameworks discussed in this thesis one has to keep in mind the differences and respect regional healthcare capacities and cultural nuances, altogether leading to more effective management of the condition worldwide.

A proactive approach to preventing secondary hypertension could include the implementation of lifestyle modification programs that are accessible community-wide and can be tailored to specific regional health profiles. Technological advancements such as telemedicine and mobile health applications should be leveraged to facilitate early diagnosis and continuous monitoring of patients at risk of secondary hypertension, especially in underserved areas.

In reviewing the diagnostic strategies for secondary hypertension as outlined by the latest ESH guidelines, a comprehensive table (see *Table 9*) has been developed to summarize the diseases or underlying causes alongside their respective diagnostic workups and expected changes in laboratory parameters. This consolidation aids in illustrating the complexity and specificity required in the diagnostic process, especially in atypical presentations as observed in the clinical case presented in this thesis. The inclusion of this table underscores the importance of tailoring diagnostic approaches to individual patient profiles, reflecting both common and uncommon aetiologies of secondary hypertension.

Table 9

Underlying cause	**Diagnostic workup**
Renal parenchymal disease	- Basic metabolic panel: Increased serum creatinine and blood urea nitrogen - Urinalysis: Proteinuria and haematuria - Renal ultrasound: Assess for abnormalities
Renovascular hypertension	- Plasma renin activity: Increased - Doppler ultrasound, MRA, CTA: Detect narrowing or abnormalities in renal arteries
Primary Aldosteronism	- Aldosterone-to-renin ratio (ARR): Increased aldosterone, decreased renin - Confirmatory tests: No suppression of aldosterone - Adrenal CT scan: Identify adenoma or hyperplasia
Cushing's Syndrome	- 24-hour urinary free cortisol: Increased - Low-dose dexamethasone suppression test: Lack of cortisol suppression

	- MRI or CT: Detect pituitary or adrenal tumours
Pheochromocytoma	- Plasma metanephrines: Increased - Urinary catecholamines: Increased - CT/MRI of abdomen: Identify adrenal tumours - Functional imaging (MIBG, PET): Localize tumour
Thyroid disorders	- TSH: Decreased in hyperthyroidism, increased in hypothyroidism - Free T4: Increased in hyperthyroidism, decreased in hypothyroidism - Thyroid ultrasound: Detect nodules or enlargement
Hyperparathyroidism	- Serum calcium: Increased - Parathyroid hormone (PTH): Increased - Imaging (Ultrasound, Sestamibi scan): Detect parathyroid abnormalities
Aortic Coarctation	- Physical examination: Blood pressure differential between arms and legs (approx. > 20 mmHg Riva Roci) - Imaging (Echocardiogram, MRI, CT angiography): Visualize aortic narrowing
Obstructive sleep apnoea (OSA)	- Clinical symptoms assessment: Daytime sleepiness, loud snoring, apnoea episodes - Overnight polysomnography
Drug-induced hypertension	- Medication history review: Identify causative agents, e.g., NSAIDS (Ibuprofen), Corticosteroids (Prednisone), Antidepressants (tricyclic antidepressants like amitriptyline and MAO inhibitors), Immunosuppressants (Cyclosporine and tacrolimus), stimulants (methylphenidate)

	- Blood pressure monitoring: Assess changes upon drug discontinuation

CONCLUSION

Combining and integrating both perspectives, the clinical pathway for managing SH could start with detailed phenotyping of patients, followed by tailored diagnostic tests as suggested by Rossi et al. For patients suspected of having a genetic component to their hypertension, the insights provided by Hedge et al. could guide further genetic testing and personalized treatment plans. This could include the use of targeted therapies that address specific molecular abnormalities, potentially improving treatment efficacy and patient outcomes.
Moreover, the discussion by Rossi et al. about the implications of untreated SH highlights the potential for serious cardiovascular complications, further reinforcing the need for timely and accurate diagnosis. Their recommendations for treatment, based on the underlying cause of SH, offer practical guidance for clinicians to manage these complex patients effectively.
In conclusion, the combination of clinical acumen and molecular insights into SH provides a comprehensive approach to a condition that, if properly managed, could significantly improve the quality of life for patients. Future research should aim to further integrate these perspectives, perhaps through interdisciplinary studies that explore the interface between clinical phenotypes and genetic markers. Such efforts could lead to more sophisticated diagnostic tools and more effective, personalized therapeutic strategies, ultimately advancing the field of hypertension management. A focus on elucidating the prevalence and mechanisms by which ENT disorders contribute to hypertension could also be beneficial. Studies with such focus could broaden the scope of diagnostic considerations and therapeutic options available to clinicians, ultimately enhancing the precision and effectiveness of hypertension management. However, prospective studies are needed to further elucidate the relationship between airway obstructions and nocturnal hypertension. Additionally, there is a need for randomized controlled trials to compare the outcomes of surgical versus medical management in secondary hypertension, not only due to airway issues, but in general. As the role of technology in diagnosing and managing hypertension continues to evolve, future studies could explore the impact of wearable technology in monitoring blood pressure variations in real-time, potentially allowing for earlier intervention in cases of secondary hypertension.

RECOMMENDATIONS

Ultimately, this thesis advocates for an enhanced model of healthcare delivery for patients with secondary hypertension. By advocating for a synthesis of clinical practice with genetic and molecular research, it calls for a paradigm shift towards more integrated, personalized care that not only treats but also anticipates the complexities of SH, as is also recommended by the 2023 European Society of Hypertension (ESH) Guidelines. This proposed paradigm would not only enhance patient outcomes, but also resonates deeply with the progressive trajectory of medical science, where precision medicine and individualized treatment strategies are increasingly becoming the cornerstone of innovative healthcare solutions and stand at the forefront of innovation and treatment.

Incorporation of the 2023 ESH Guidelines into Secondary Hypertension Research

The 2023 European Society of Hypertension (ESH) Guidelines provide comprehensive updates that are crucial for the management of secondary hypertension and offer a detailed exploration of the diagnostic work-up, treatment strategies, and the importance of identifying the underlying causes of secondary hypertension.

The ESH Guidelines emphasize the necessity of a thorough and systematic approach to diagnosing secondary hypertension. This involves:

1. Initial Assessment: Complete history taking, physical examination, and baseline laboratory tests.
2. Targeted Investigations: Depending on the suspected underlying cause, more specific tests are recommended. For example, renal ultrasound for renovascular hypertension, sleep studies for suspected sleep apnoea, and adrenal imaging for suspected endocrine causes.

These guidelines reinforce the case study discussed in this thesis, where a comprehensive diagnostic work-up led to the identification of a nasal polypus as a rare cause of secondary hypertension. An approach of using detailed imaging and specialized tests to confirm the diagnosis is supported by the Guidelines and was proven to be critical in the effective management of the patient's condition.

The guidelines also outline updated treatment protocols that focus on treating the underlying cause of hypertension, rather than just managing symptoms, such as the use of Angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) as pharmacological management of renovascular hypertension caused by renal artery stenosis and the use of Percutaneous transluminal renal angioplasty (PTRA) with or without stenting as surgical treatment of renal artery stenosis. As was mentioned before, the efficacy of pharmacological versus surgical treatment has yet to be explored. For Obstructive sleep apnoea (OSA) a device-based treatment by continuous positive airway pressure (CPAP) therapy is the primary treatment, another treatment, which entirely dependent on patient compliance and understanding of the disease are lifestyle modifications such as weight loss and positional therapy, which can also help reduce the severity of OSA and, consequently, improve blood pressure control. The list is not exhaustive, these are just a few examples taken from the 2023 ESH guidelines.

The treatment strategies from the guidelines highlight the importance of a precise diagnosis in guiding effective management of secondary hypertension. By targeting the specific aetiologies, these tailored treatments not only manage the symptoms of hypertension but also address the primary health issues, thereby improving overall patient outcomes.
Such cause-specific treatment approach is exemplified in the clinical case within this thesis, where surgical removal of the nasal polypus led to a significant improvement in the patient's hypertension. Moreover, the guidelines advocate for the integration of lifestyle modifications and pharmacotherapy tailored to the specific cause of secondary hypertension. This holistic approach not only aligns with the treatment strategy used in the presented case but also highlights the importance of personalized medicine in managing especially the complex cases of secondary hypertension. Lastly, the educational emphasis of the ESH Guidelines resonates with the academic purpose of this thesis. By providing a clear, structured approach to both diagnosing and managing secondary hypertension, the guidelines serve as a valuable resource for healthcare professionals at all levels.

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