Schilddrüse und Hypertonie

Arterielle Hypertonie
Pulmonale Hypertonie

Hans-Jürgen Gallowitsch

Ursachen der sekundären Hypertonie nach Altersgruppe

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Table 4. Most Common Causes of Secondary Hypertension by Age*

Age groups	*Percentage of patients who have hypertension with an underlying cause*	*Most common etiologies†*
Children (birth to 11 years)	70 to 85	Renal parenchymal disease Coarctation of the aorta
Adolescents (12 to 18 years)	10 to 15	Renal parenchymal disease Coarctation of the aorta
Young adults (19 to 39 years)	5	Thyroid dysfunction Fibromuscular dysplasia Renal parenchymal disease
Middle-aged adults (40 to 64 years)	8 to 12	Hyperaldosteronism Thyroid dysfunction Obstructive sleep apnea Cushing syndrome Pheochromocytoma
Older adults (65 years and older)	17	Atherosclerotic renal artery stenosis Renal failure Hypothyroidism

*—*Excluding dietary and drug causes and the risk factor of obesity.*
†—*Listed in approximate order of frequency within groups.*

Adapted with permission from Viera AJ, Neutze DM. Diagnosis of secondary hypertension: an age-based approach. Am Fam Physician. *2010;82(12):1473, with additional information from references 4, 14, and 29.*

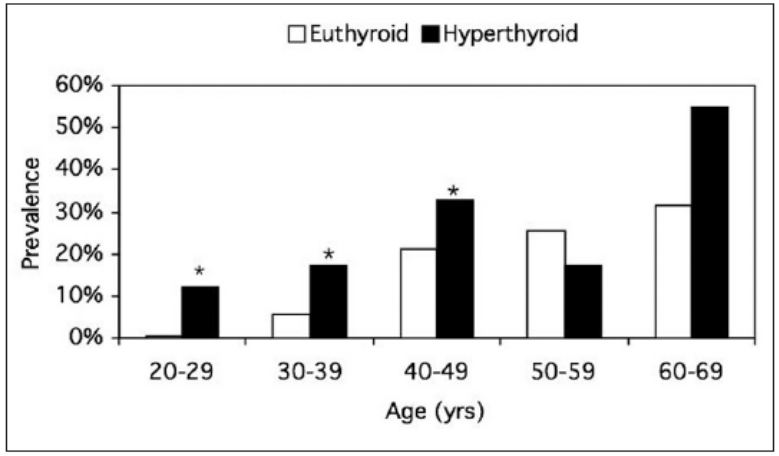

*Figure 2. Prevalence of hypertension in 594 euthyroid and 446 hyperthyroid patients. The prevalence of hypertension was significantly higher in patients younger than 50 years of age. *p<0.05. Reproduced with permission from* Endocrinol Metab Clin North Am. *1994;23:379–386.*[18]

Hyperthyreose und Arterielle Hypertonie

Klinische Evidenz

Hyperthyreose und kardiale Pumpfunktion

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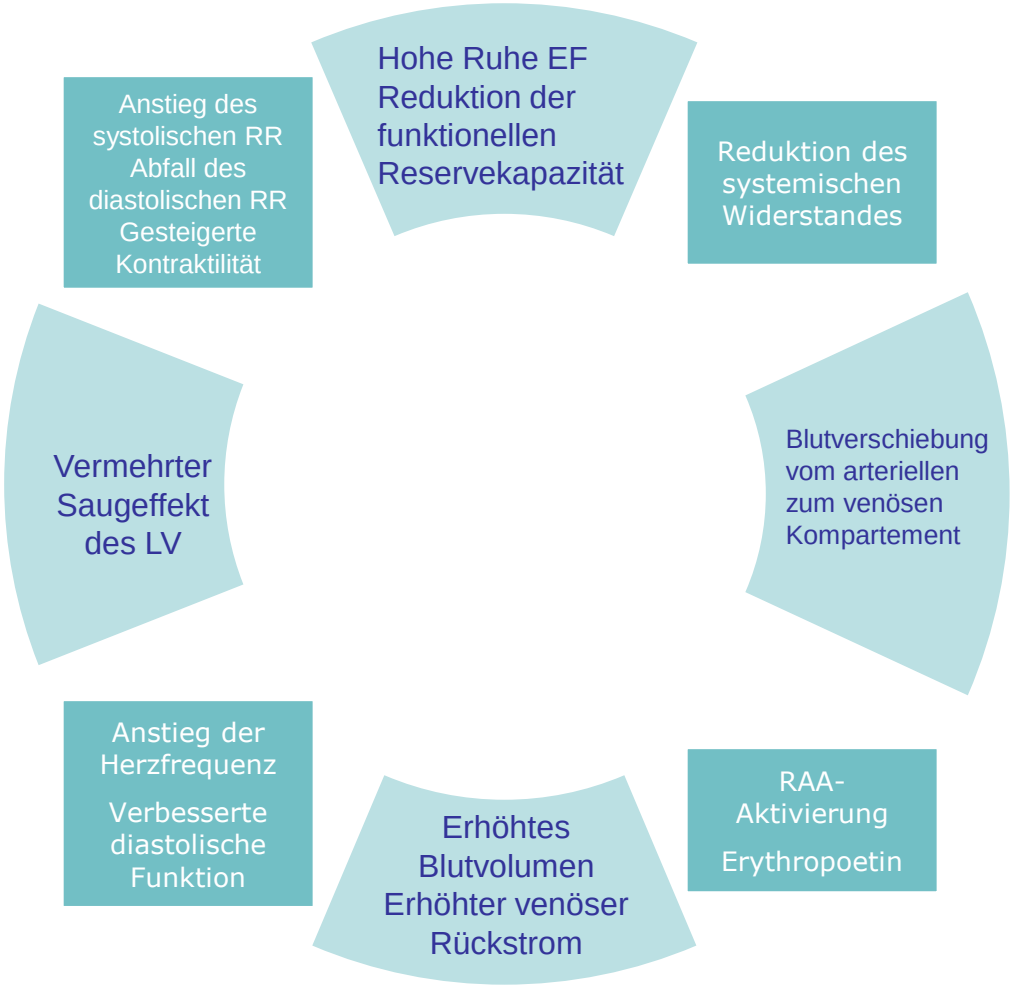

Hyperthyreose			
Vorlast			⇑
	peripherer Gefäßwiderstand		⇓
		venöser Rückstrom	⇑
		Perfusionsdruck der Niere	⇓
	RAA-Aktivierung	Blutvolumen	⇑
	Erythyropoetin	Erythrozytenvolumen	⇑
	LV Volumen		⇒
		Relaxation beschleunigt	
		diastolische Füllungsindices	⇑
Nachlast			⇓
	peripherer Gefäßwiderstand		⇓
	systolischer Druck		⇑
	Herzfrequenz		⇑
	endsystolische Wandspannung		⇒
Kontraktilität			⇒⇑

Hyperthyreose und sekundäre Hypertonie

Manifeste Hyperthyreose häufige Ursache einer isolierten systolischen Hypertonie

- Ca. ein 1/3 aller manifesten Hyperthyreosen mit Erhöhung des systolischen RR assoziiert (Prisant LM, Gujral JS, Mulloy AL (2006) Hyperthyroidism: a secondary cause of isolated systolic hypertension. J Clin Hypertens 8: 596–599)

Hyperthyreose und sekundäre Hypertonie

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Nach Therapie der Hyperthyreose:

- Systolischer RR und Herzfrequenz nehmen nach Behandlung der HT ab, deutlicher bei jüngeren Patienten

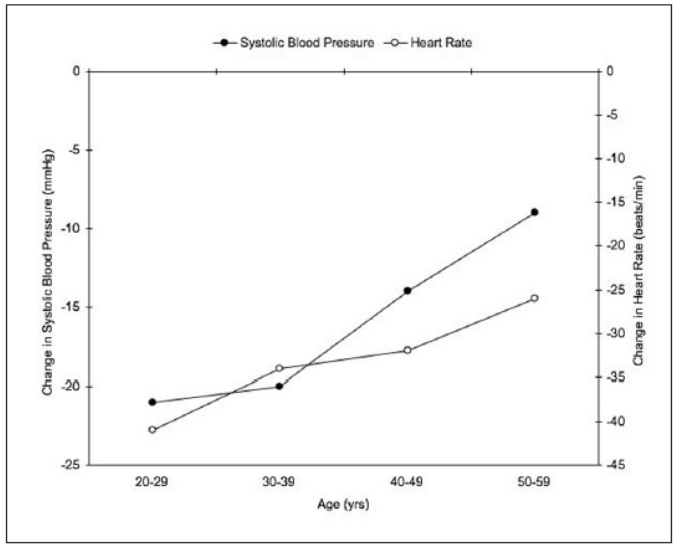

Figure 3. Change in systolic blood pressure and heart rate in 321 hyperthyroid patients treated with anti-thyroid drugs, radioactive iodine, or subtotal thyroidectomy. Systolic blood pressure and heart rate decreased with treatment of hyperthyroidism, but there was a greater reduction in both parameters in younger patients. Data derived from J Am Geriatr Soc. *1985;33:19-22.*[17]

Arterielle Hypertonie und latente Funktionsstörung

Blood pressure levels in patients with subclinical thyroid dysfunction: a meta-analysis of cross-sectional data

Yunfei Cai[1,2], Yongkui Ren[3] and Jingpu Shi[1,2]

The relationship between subclinical thyroid dysfunction and blood pressure is controversial and has received insufficient attention. The aim of this study was to assess whether blood pressure levels in patients with subclinical thyroid dysfunction differ from those of euthyroid subjects. A meta-analysis of all cross-sectional studies was performed to compare the blood pressure levels in patients with subclinical thyroid dysfunction with those of healthy controls. A computer-based online retrieval of databases (MEDLINE and EMBASE) and manual searches were undertaken to identify articles that addressed the association between subclinical thyroid dysfunction and blood pressure levels and were published through 2010, using no language restrictions. The meta-analysis was performed using STATA 11 (Stata). Seven cross-sectional studies were examined. In patients with subclinical hypothyroidism, the pooled estimate of the weighted mean difference (WMD) of increased blood pressure revealed a significant difference in both systolic blood pressure (SBP; WMD with 95% confidence interval (CI) 1.89 mm Hg (0.98–2.80), $P<0.05$) and diastolic blood pressure (DBP; WMD with 95% CI 0.75 mm Hg (0.24–1.27), $P<0.05$). However, in patients with subclinical hyperthyroidism, the pooled estimate of the WMD of increased blood pressure revealed no significant difference in SBP (WMD with 95% CI −0.75 mm Hg (−1.81 to 0.31)) or DBP (WMD with 95% CI −0.64 mm Hg (−2.36 to 1.08)). The present meta-analysis indicates that subclinical hypothyroidism is associated with increased SBP and DBP, whereas subclinical hyperthyroidism is not. Further investigation is needed to confirm blood pressure levels in patients with subclinical thyroid dysfunction.

Hypertension Research (2011) **34**, 1098–1105; doi:10.1038/hr.2011.91; published online 28 July 2011

Keywords: blood pressure; hyperthyroidism; hypothyroidism; meta-analysis; thyroid disease

Exogene latente Hyperthyreose (Suppressionstherapie)

Exogene latente Hyperthyreose (Suppressionstherapie):

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- **Keine signifikante Änderung**
  - des systolischen und diastolischen Blutdrucks,
  - des systemischen Gefäßwiderstands sowie
  - der autonomen kardialen Funktion
- **Auswirkungen:**
  - **In Ruhe** marginal höhere tägliche und nächtliche Herzfrequenz,
  - Zunahme der linksventrikulären Muskelmasse
  - beeinträchtigte Relaxation bei erhaltener systolischer Funktion
  - SVES häufiger, Häufigkeit ventrikulärer Herzrhythmusstörungen (HRS) nicht erhöht

Exogene latente Hyperthyreose (Suppressionstherapie):

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- **Signifikant beeinträchtigte Belastungskapazität**, in Bezug auf
  - das erreichte Belastungsmaximum
  - die Belastungsdauer
  - die maximale Sauerstoffaufnahme
  - Absenken der anaeroben Schwelle
  - Auswurfleistung gegenüber dem gesunden Vergleichskollektiv unter Belastung reduziert
- Eine β-Blockade über 6 Monate führt zur
  - Verminderung der mittleren Herzfrequenz,
  - Abnahme der SVES und auch einer therapieinduzierten Flimmerarrhytmie
  - Reduktion des LV Massen-Index

Hypothyreose und Arterielle Hypertonie

Klinische Evidenz

Hypothyreose		
Peripherer Gefäßwiderstand		⇑
Systolische Funktion		⇒
Diastolisches Füllungsverhalten	PEP	⇑
	PEP/ET	⇑
	myokardiale Steifigkeit	⇑
Mittlerer arterieller Druck		⇒
	systolischer Druck	⇓
	diastolischer Druck	⇑
Herzfrequenz		⇓
Kontraktilität	unter Ruhe	⇒
	unter Belastung	⇓
LV Masse		⇒⇑
Stoffwechsel	Gesamtcholesterin	⇑
	LDL	⇑
	LP-A	⇑
	Homocystein	⇑
	CRP	⇑

Hypothyreose

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- Kardiale Auswirkungen:
  - Bradykardie
  - Anstieg des systemischen Gefäßwiderstandes
  - Verminderter kardialer Output
  - Mittlere Blutdruck weitgehend konstant
    - Anstieg des diastolischen Blutdrucks
    - Verringerung systolischer Blutdruckwerte
  - Zunahme der myokardialen Steifigkeit und diastolische Dysfunktion
- **Verminderte LV Funktion in Ruhe beruht eher auf einer Abnahme der Volumslast als auf einer Veränderungen der myokardialen Kontraktilität**

Latente Hypothyreose und kardiovaskuläre Dysfunktion.

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- In Ruhe
  - systolische kontraktile Funktion nicht beeinflusst
    - Ruhefrequenz normal
    - systolischen Zeitintervalle normal
  - Diastolische Funktionstörung
    - Verlängerung der isovolumetrischen Relaxationszeit
- Unter Belastung
  - systolische Funktionsstörung
    - signifikant niedrigeres Schlagvolumen
    - verringerte maximale aortale Flussgeschwindigkeit
    - Sauerstoffaufnahme pro Herzschlag (Sauerstoffpuls) sowohl im Bereich der anaeroben Schwelle als auch bei maximaler Belastungskapazität reduziert
- Veränderungen nach L-Thyroxin-Therapie reversibel

Latente Hypothyreose und kardiovaskuläres Risiko.

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- Substitutionsbehandlung mit Levothyroxin
  - reduziert das Gesamtcholesterin, Lp-A und das LDL, insbesondere bei Patienten mit hohem Cholesterinspiegel und hohem bTSH Ausgangswert
  - verbessert den Gefäßwiderstand und die myokardiale Kontraktilität
  - bei bereits angiographisch verifizierter KHK verhindert die Substitutionsbehandlung mit Levothyroxin die weitere Progression bei hypothyreoten Patienten

Evaluation of biochemical, hematological, and thyroid function parameters in nondipper and dipper hypertensive patients

Ibrahim Akpinar, Nurcan Basar, Nihat Sen, Halil Lutfu Kisacik

Wien Klin Wochenschr (2012) 124:439–443

- 470 Hypertonie-Patienten
- Werte von Nüchternblutzucker, Harnstoff, Kreatinin, Harnsäure, SGOT, SGPT, gamma GT, Gesamt Eiweiß, Lipidprofile, Na, K, Hb, Leukozyten, Thrombozyten, mittleres Thrombozyten Volumen, Thyreotropin (TSH), freien Schilddrüsenhormonen,
- 24 h Blutdruck Monitoring.
- Non- Dipper Gruppe: 398 Patienten (ohne physiologischem nächtlichem RR Abfall),
- Dipper Gruppe: 72 Patienten

Table 2. Comparison of thyroid function tests in two groups

	Dipper HT Group (n=72)	Nondipper HT Group (n=398)	P value
TSH (µIU/mL)	1.69±1.14	2.11±1.84	0.041
Free T3 (pg/mL)	3.28±1.23	2.97±0.53	0.016
Free T4 (ng/dL)	1.32±0.39	1.20±0.44	0.009

TSH levels were statistically higher in the nondipper hypertensive group than the dipper hypertensive group, and free T3 and T4 levels were lower

- Ergebnisse:
  - kein statistischer Unterschied zwischen beiden Gruppen bezüglich Alter, Geschlecht, und der erhobenen biochemischen und hämatologischen Parameter
  - **signifikant höhere TSH-, und signifikant niedrigere freie Thyroxin- und Trijodthyronin- Werte bei den Non-Dipper Hypertonie Patienten.**
  - Möglicherweise mit einem Abfall der Compliance der Venenwand in Zusammenhang

Arterielle Hypertonie und Schilddrüse

Blood pressure levels in patients with subclinical thyroid dysfunction: a meta-analysis of cross-sectional data

Yunfei Cai[1,2], Yongkui Ren[3] and Jingpu Shi[1,2]

The relationship between subclinical thyroid dysfunction and blood pressure is controversial and has received insufficient attention. The aim of this study was to assess whether blood pressure levels in patients with subclinical thyroid dysfunction differ from those of euthyroid subjects. A meta-analysis of all cross-sectional studies was performed to compare the blood pressure levels in patients with subclinical thyroid dysfunction with those of healthy controls. A computer-based online retrieval of databases (MEDLINE and EMBASE) and manual searches were undertaken to identify articles that addressed the association between subclinical thyroid dysfunction and blood pressure levels and were published through 2010, using no language restrictions. The meta-analysis was performed using STATA 11 (Stata). Seven cross-sectional studies were examined. In patients with subclinical hypothyroidism, the pooled estimate of the weighted mean difference (WMD) of increased blood pressure revealed a significant difference in both systolic blood pressure (SBP; WMD with 95% confidence interval (CI) 1.89 mm Hg (0.98–2.80), $P<0.05$) and diastolic blood pressure (DBP; WMD with 95% CI 0.75 mm Hg (0.24–1.27), $P<0.05$). However, in patients with subclinical hyperthyroidism, the pooled estimate of the WMD of increased blood pressure revealed no significant difference in SBP (WMD with 95% CI −0.75 mm Hg (−1.81 to 0.31)) or DBP (WMD with 95% CI −0.64 mm Hg (−2.36 to 1.08)). The present meta-analysis indicates that subclinical hypothyroidism is associated with increased SBP and DBP, whereas subclinical hyperthyroidism is not. Further investigation is needed to confirm blood pressure levels in patients with subclinical thyroid dysfunction.

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Pulmonale Hypertonie und Schilddrüse

Pulmonale Hypertonie

Table 1. The Revised World Health Organization Classification of Pulmonary Hypertension.*

Group I. Pulmonary arterial hypertension
- Idiopathic (primary)
- Familial
  - Related conditions: collagen vascular disease, congenital systemic-to-pulmonary shunts, portal hypertension, HIV infection, drugs and toxins (e.g., anorexigens, rapeseed oil, L-tryptophan, methamphetamine, and cocaine); other conditions: thyroid disorders, glycogen storage disease, Gaucher's disease, hereditary hemorrhagic telangiectasia, hemoglobinopathies, myeloproliferative disorders, splenectomy
- Associated with significant venous or capillary involvement
  - Pulmonary veno-occlusive disease
  - Pulmonary-capillary hemangiomatosis
- Persistent pulmonary hypertension of the newborn

Group II. Pulmonary venous hypertension
- Left-sided atrial or ventricular heart disease
- Left-sided valvular heart disease

Group III. Pulmonary hypertension associated with hypoxemia
- Chronic obstructive pulmonary disease
- Interstitial lung disease
- Sleep-disordered breathing
- Alveolar hypoventilation disorders
- Chronic exposure to high altitude
- Developmental abnormalities

Group IV. Pulmonary hypertension due to chronic thrombotic disease, embolic disease, or both
- Thromboembolic obstruction of proximal pulmonary arteries
- Thromboembolic obstruction of distal pulmonary arteries
- Pulmonary embolism (tumor, parasites, foreign material)

Group V. Miscellaneous
- Sarcoidosis, pulmonary Langerhans'-cell histiocytosis, lymphangiomatosis, compression of pulmonary vessels (adenopathy, tumor, fibrosing mediastinitis)

- Permanente Erhöhung des Pulmonalarteriellen Druckes auf mehr als 25 mm Hg in Ruhe oder mehr als 30 mm Hg bei Belastung,
- Histologisch Intimafibrose, verdickte Media, Verschluss pulmonaler Arteriolen und Prädominanz plexiformer Läsionen

Farber HW, Loscalzo J. Pulmonary arterial hypertension. N Engl J Med 2004;351:16553– 65.

Hypothyreose und pulmonale Hypertonie

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durch mehrere Faktoren bedingt:
• Prävalenz der Hypothyreose bei primärer pulmonaler Hypertonie 10-24 % (D.B. Badesch et al. Ann. Intern. Med. 119, 44–46 (1993); R.G. Chin, J. Fisher, Cardiovasc. Rev. Rep. 9, 789–796 (1986); A.L. Curnock et al. Am. J. Med. Sci. 318, 289–292 (1999)
• Autoimmunität als bestimmender Faktor – systemische vaskuläre Inflammation – Remodeling der pulmonalen Gefässe
• Ca. 50 % der Patienten mit PAH und AITH haben auch Kollagenosen (CREST Syndrom, RA, Sklerodermie)
• Östrogeneinnahme, AITH und Adipositas begünstigt PAH, • Höherer BMI von hypothyreoten Patienten begünstigt systemische vaskuläre Inflammation

Hypothyreose und PAH

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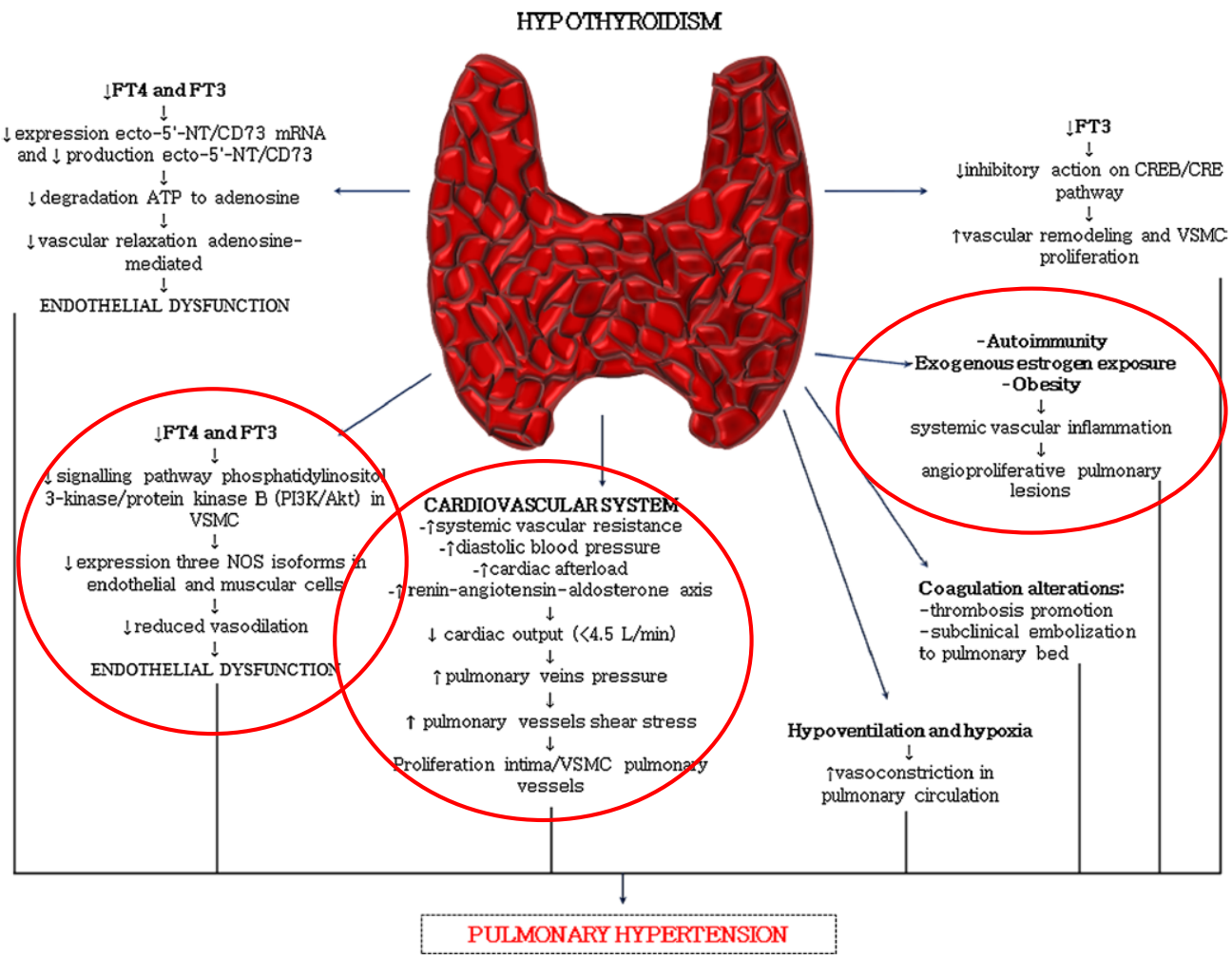

Fig. 1 Possible mechanisms involved in the genesis of pulmonary arterial hypertension in patients suffering from hypothyroidism. *ATP* adenosine triphosphate, *CREB/CRE* cyclic adenosine monophosphate response element (CRE) binding protein (CREB), *FT3* free tri-iodothyronine, *FT4* free free thyroxine, *NOS* nitric oxide synthase, *VSMC* vascular smooth muscle cells

Pietro Scicchitano et al. Pulmonary hypertension in thyroid diseases, Endocrine (2016) 54:578–587

Hyperthyreose und pulmonale Hypertonie

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Prävalenz der Hyperthyreose bei primärer pulmonaler Hypertonie
• 41-47 % (M. Marvisi et al., Respir. Med. 96, 215–220 (2002); M. Marvisi, et al. Eur. J. Intern. Med. 17, 267–271 (2006); R. Alca´zar et al. Rev. Esp. Cardiol. 48, 142–144 (1995), C.W. Siueta al. J. Clin Endocrinol. Metab. 92, 1736–1742 (2007), J. Merce et al. Am. J. Med. 118, 126–131 (2005); C.M. Trapp et al. J. Clin. Endocrinol. Metab. 97, 2217–2222 (2012); R. Obeid et al. BMJ Case Rep. (2012). doi: 10.1136/bcr. 02.2012.5939; D. O'Donovan et al. Ir. Med. J. 90, 147–148 (1997); B. Agraouet al. Arch. Mal. Coeur Vaiss. 89, 765–768 (1996)
• Auch bei pädiatrischen Patienten
• Abfall des PAP nach thyreostatischer Therapie J. Merce et al. Am. J. Med. 118, 126–131 (2005)
• Kombination begünstigt akute kardiale Dekompensation, erfordert rasche Normalisierung der SD-Werte

Änderung des PAP nach Therapie der Hyperthyreose

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TABLE 1. Changes in pulmonary artery pressures after the treatment of hyperthyroidism

Author	n	Age/sex	Etiology	Pre-Rx pressures (mm Hg)	Post-Rx pressures (mm Hg)	Treatment	Duration of Rx (mo)
Virani et al[4]	2	40/F	Graves' AF	73	38	Metoprolol, PTU, ^{131}I	6
		38/F	Graves'	78	41	Metoprolol, PTU, ^{131}I	5
Thurnheer et al[5]	4	26/F	Graves'	35	21	Thiamazole, ^{131}I	6
		79/F	Multinodgoiter	34	26	^{131}I	2
		54/F	Graves'	56	35	PTU	1
		24/M	Graves'	33	21	Thiamazole	12
Marvisi et al[6]	50	51/F†	Graves' (n = 33)	34.3 ± 3.2	29.2 ± 3.3	Methimazole	0.5
		(68%)	Nodular goiter (n = 17)	34.3 ± 3.0	34.1 ± 2.9	Partial thyroidectomy	
Ismail[7]	1	56/F	Graves'	75	45	Methimazole	0.25–0.75
Lozano and Sharma[8]	1	29/F	Graves'	51	26	PTU, KI Subtotal thyroidectomy	NR
*Nakchbandi et al[9]	1	46/F	Graves'	78*	32	^{131}I PTU	7
Hegazi et al[10]	1	43/F	Graves	70	55	Carbimazole	14
Armigliato et al[11]	16	47/F	Graves' (15)	*M* = 37.4	*M* = 28	Methimazole	9
		(50%)	Multinod goiter (1)		^{131}I Surgery		
Alcázar et al[12]	1	28/F		62	45	Neocarbimazole	NR
Nduyao et al[13]	1	49/F	Graves'	68	30	Carbimazole, ^{131}I	NR
Agraou et al[14]	1	48/F	NR	60	27	Thyroidectomy	NR
Mozo et al[15]	1	49/F	Toxic multinod goiter	65	45	Thyroidectomy	NR
*Moraza et al[16]	1	48/F	Graves'	68*	39		NR
Souroush-Yari et al[17]	3	41/M	Graves'	57	36	PTU, RAI	9
		68/M	Graves'	68	32	Methimazole, RAI	24
		59/M	Graves'	51	34	PTU, RAI	24
Polo Romero et al[18]	1	34/F		50	19	PTU	NR
Yazar et al[19]	25	49.8/F	Graves' (7)	*M* = 30.4	24.4	PTU	6
		(60%)	Toxic nodular goiter (18)			RAI or surgery	
Paran et al[20]	1	38/F	Graves' A-fib	70	48	Propranolol, PTU dexamethasone	0.5
Mercé et al[21]	39	52/F	Hyperthyroidism	36 ± 10	29 ± 8		6
		(72%)		(n = 33)			
Siu et al[22]	19	44/F†	Graves'	47 ± 2	34 ± 2	Carbimazole, PTU, RI	6
		(66%)					
Hamagawa et al[23]	1	83/F		103	29	Methimazole	NR

* Pulmonary artery pressure measured by pulmonary artery catheterization.
† Mean age and percentage of females of the total subjects in the study (not all had both hyperthyroidism and pulmonary hypertension).
PTU, propylthiouracil; KI, potassium iodide; NR, not reported.

Hyperthyreose und PAH

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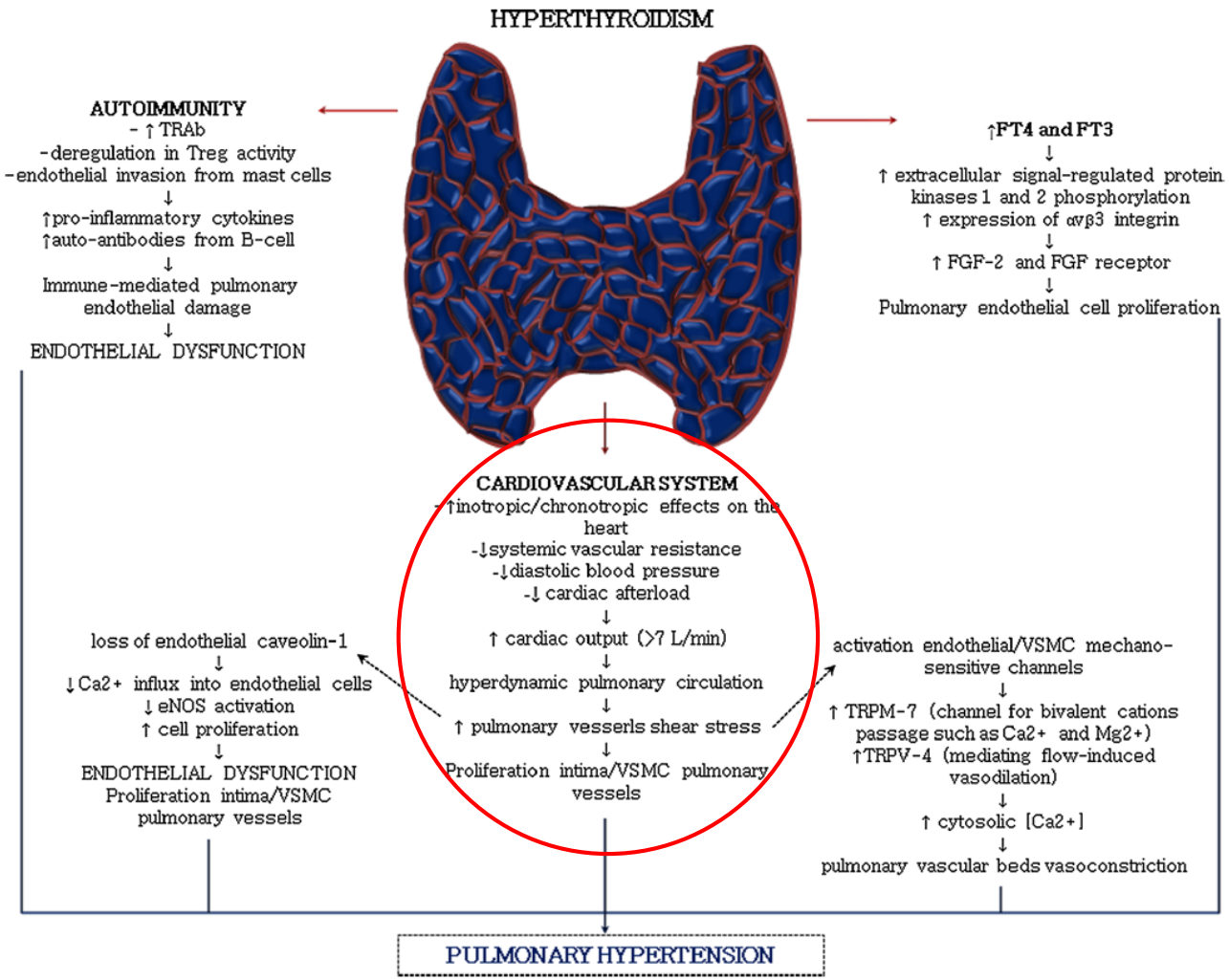

Fig. 2 Possible mechanisms involved in the genesis of pulmonary arterial hypertension in patients suffering from hyperthyroidism. Ca^{2+} calcium ion, *eNOS* endothelial nitric oxide synthase, *FGF* fibroblast growth factor, *FT3* free triiodothyronine, *FT4* free thyroxine, *TRAb* thyroid stimulating hormone receptor antibody, *Treg* regulatory T-cell lymphocytes, *TRPM-7* melastatin-related transient receptor potential-7, *TRPV-4* vanilloid-related transient receptor potential-4, *VSMC* vascular smooth muscle cells

Pietro Scicchitano et al. Pulmonary hypertension in thyroid diseases, Endocrine (2016) 54:578–587

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Hyperthyroidism and Pulmonary Hypertension: An Important Association

Sailaja Vallabhajosula, MD, Saba Radhi, MD, Cihan Cevik, MD, Raed Alalawi, MD, Rishi Raj, MD and Kenneth Nugent, MD

- **Abstract:** Pulmonary hypertension is a complex disorder with multiple etiologies. The World Health Organization Group 5 (unclear multifactorial mechanisms) includes patients with thyroid disorders. The authors reviewed the literature on the association between hyperthyroidism and pulmonary hypertension and identified
- 20 publications reporting 164 patients with treatment outcomes.
- The systolic pulmonary artery (PA) pressures in these patients ranged from 28 to 78 mm Hg.
- They were treated with antithyroid medications, radioactive iodine and surgery. The mean pretherapy PA systolic pressure was 39 mm Hg; the mean posttreatment pressure was 30 mm Hg.
- Pulmonary hypertension should be considered in hyperthyroid patients with dyspnea.
- All patients with pulmonary hypertension should be screened for hyperthyroidism, because the treatment of hyperthyroidism can reduce PA pressures, potentially avoid the side-effects and costs with current therapies for pulmonary hypertension and limit the consequences of untreated hyperthyroidism.
- However, the long-term outcome in these patients is uncertain, and this issue needs more study. Changes in the pulmonary circulation and molecular regulators of vascular remodeling likely explain this association.

- **[Am J Med Sci 2011;342(6):507–512.]**

Bei allen Patienten mit Dyspnoe und Hyperthyreose sollte an das Vorliegen einer pulmonalen Hypertonie gedacht werden.

Alle Patienten mit pulmonaler Hypertonie sollten hinsichtlich einer Hyperthyreose untersucht werden. Behandlung der Hyperthyreose reduziert PAP, reduziert Nebenwirkungen und Kosten einer Therapie der pulmonalen Hypertonie