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Oral thyroid hormone pretreatment in left ventricular dysfunction

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Abstract

Objective: The aim of the present study was to determine whether pretreatment with oral thyroid hormone had beneficial effects in cardiac function and morbidity and mortality after cardiac operations. **Methods**: Eighty patients undergoing coronary artery bypass grafting with a preoperative left ventricular ejection fraction (LVEF) less than 30% scheduled for elective coronary bypass grafting agreed to participate in this prospective, randomized trial. The triiodothyronine (T_3) (Group I) and control groups (Group II) were equally divided. Patients randomized to the T_3 group received T_3 125 μg/day orally for 7 days preoperatively and from the first postoperative day till the discharge. Outcome variables included perioperative hemodynamic data, inotropic requirements, morbidity and mortality. Hemodynamic data were collected before induction of anesthesia and following every 4 h. The thyroid profile was determined upon admission, after the induction of anesthesia, 5 min after the start of cardiopulmonary bypass (CPB) and after hourly intervals and after 24th hour, at 24 h intervals till the 120th hour. **Results**: There were 6 deaths, three in each group. Patients in the T_3 group demonstrated a higher cardiac index than patients in the placebo group in the entire post-CPB periods ($P<0.01$). Mean inotropic requirements remained lower in the T_3 group than in the placebo group ($P<0.001$). **Conclusions**: Although our study stresses the benefits of oral T_3 administration on the hemodynamic and prognostic parameters in patients with impaired left ventricular function and undergoing CABG weakly, it may warrant further much larger scaled studies that can reach statistical significance.
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Keywords: Thyroid hormone; Left ventricular dysfunction; Coronary artery bypass surgery

1. Introduction

Thyroid hormone has long been known to exert profound effects on the cardiovascular system. The physiologic effects of thyroid hormone result from the action of both triiodothyronine (T_3) and tetraiodothyronine (T_4) on variety of organ systems. These include a decrease in peripheral vascular resistance and positive chronotropic and inotropic effects [1,2]. Increasing number of patients with underlying chronic left ventricle (LV) dysfunction are presenting for cardiac surgical procedures [3]. In many of these patients, this preexisting LV dysfunction may be exacerbated after hypothermic cardioplegic arrest and rewarming. It has been demonstrated that patients with chronic LV dysfunction have an associated decrease in the level of active form of thyroid hormone, 3,5,3 triiodo-L- thyronine (T_3) [4,5]. Both clinical and experimental studies have demonstrated that increased circulating levels of T_3 improved LV pump function in normal myocardium as well as after acute ischemic injury to the myocardium [6].

In spite of the numerous studies on the intravenous use, there is not any study showing the oral use of thyroid hormone for the pretreatment of the patients undergoing open heart surgery with impaired left ventricular function. The aim of the present study was to determine whether pretreatment with oral T_3 had beneficial effects in cardiac function, morbidity and mortality after cardiac operations.

2. Material and methods

2.1. Patient selection criteria

Eighty patients undergoing coronary artery bypass grafting with a preoperative left ventricular ejection fraction

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(LVEF) less than 30% scheduled for elective coronary bypass grafting agreed to participate in this prospective, randomized double blind placebo controlled trial. Exclusion criteria included valvular surgery, history of thyroid disease or thyroid replacement therapy, evolving myocardial infarction, preoperative insertion of an intra-aortic balloon pump (IABP), and emergency operation. The patients were advised of the details of the study and informed consents were obtained. Institutional Review Board approval was also received.

Subjects were randomly assigned into two groups. The T_3 (Group I) and placebo (Group II) groups were equally divided. Block randomization was used to keep the number subjects in two groups closely balanced. Patients randomized to the T_3 group received T_3 125 μg/day (Cynomel® 25 mcg, SmithKline-Beecham-Enila) orally for 7 days preoperatively and on the first postoperative day. T_3 was given in the same dose till the discharge. The pre- and perioperative information documented on each patient included age, sex and the number of grafts performed. Outcome variables included perioperative hemodynamic data, inotropic requirements, morbidity and mortality. Morbidity parameters included the prevalence of atrial fibrillation, myocardial ischemia and infarction, and mechanical assistance (IABP).

Hemodynamic data were collected before induction of anesthesia and following every 4 h including the 24th hour. Mixed venous oxygen saturation was determined by standard blood gas analysis of pulmonary arterial-blood samples. Cardiac output was determined by thermodilution and derived measurements were done. The thyroid profile was determined upon admission, 5 min after the start of cardiopulmonary bypass (CPB) and after hourly intervals and after 12th hour, at 24 h intervals till the 120th hour.

Perioperative myocardial ischemia/infarction was diagnosed electrocardiographically and by increments of the creatine kinase MB fraction ($>10\%$) and aspartate aminotransferase (>100 mg/dl).

2.2. Operative technique

Patients were brought to the operating room where lines were placed after institution of general endotracheal high-dose narcotic anesthesia. A Swan-Ganz catheter (Baxter Healthcare Corp., Edwards Division, Santa Ana, CA) was inserted in each case. A standard median sternotomy incision was used in all patients and no minimally invasive technique was used. Following systemic heparinization, arterial cannulation to the ascending aorta and venous cannulation with a two-stage canulla to the right atrial appendage were performed, and all the operations were done with moderate hypothermic CPB with membrane oxygenators. Multi-dose antegrade cold blood cardioplegia and topical hypothermia were used for myocardial preservation.

All distal coronary anastomosis were performed during the single aortic cross-clamp period. Proximal anastomosis were done with partial aortic occlusion during rewarming.

2.3. Biochemical measurements

Serum thyroid stimulating hormone (TSH), free thyroxine (fT_4)and free triiodothyronine (fT_3) were analyzed at the time the blood was collected. Their levels were measured by fluorescent microparticle enhanced immunoassay (Abbot Laboratories Ltd, Maidenhead, UK).

2.4. Statistical analysis

Data were presented as mean ± standard deviation. Continuous variables were analyzed by Student's *t* and Mann Whitney *U*-test, where appropriate. Chi-square and Fisher's Exact test were used to test categorical variables between two groups. Differences among different time points for the continuous variables were evaluated by repeated-measures ANOVA and Friedman two-way analysis of variance by ranks, where applicable. When the *P*-value from the Friedman test statistics is statistically significant, multiple-comparison test was used to know which time point differs from others [7]. To control type I error, Bonferroni adjustment was applied for multiple comparisons.

3. Results

3.1. Patient demographics

As summarized in Table 1, the two groups were not statistically different with respect to a variety of preoperative and intraoperative factors, the majority of the initial intraoperative hemodynamics, and duration of CPB and aortic cross-clamping.

Table 1
Patient demographics

	T_3 group	Placebo group	*P*
Number of patients	40	40	
Age (years)	65±3.2	66±2.8	0.14
Female	12	10	0.62
Preoperative characteristics			
Hypertension	7	8	0.78
Unstable angina	5	4	1.00
Ejection fraction (EF)%	29.2±2.8	28.8±2.3	0.49
TSH (mU/l)	1.5±0.8	1.3±0.9	0.21
Free T3 (pmol/l)	3.5±1.2	3.8±1.1	0.32
Free T4 (pmol/l)	14.5±0.9	14.8±1.4	0.37
Intraoperative characteristics			
CPB time (min)	125±32	115±10	0.06
Aortic cross-clamp time (min)	55±18	50±19	0.06
Number of grafts	3.7±2.1	3.4±1.8	0.49

CPB, cardiopulmonary bypass; TSH, thyroid stimulating hormone.

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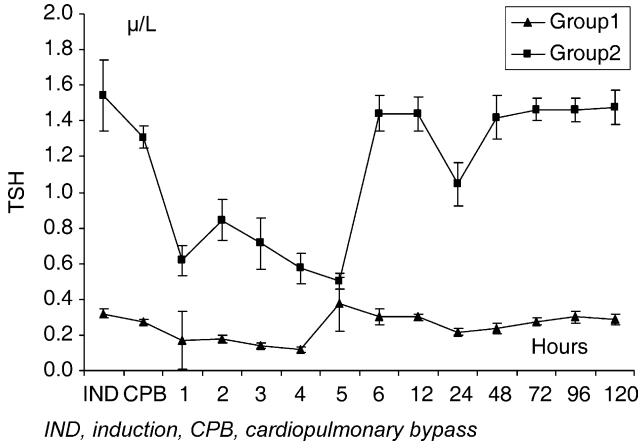


Fig. 1. Time course of the serum concentrations of the thyroid stimulating hormone.

3.2. Plasma TSH levels

There was a significant difference between Groups I and II in regard to the levels of TSH before the initiation of CPB ($P<0.001$). In both groups there was a significant fall in TSH ($P<0.001$) once CPB had been established and the levels remained low till the 5th hour. But, the mean fall of TSH was significantly higher in regard to the baseline values in Group I throughout the first 5 h ($P<0.001$). In the 6th hour, the levels began to rise in both groups ($P<0.001$) but the increments did not reach statistical significance between the two groups ($P>0.05$) throughout the remainder of the study. The return to baseline values was observed after 72nd hours in both groups (Fig. 1).

3.3. Plasma free T_3 levels

The fT_3 level was significantly higher in the T_3 treated patients on the induction of anesthesia. After the initiation of CPB there were significant falls in T_3 levels in both groups ($P<0.001$). The significant fall sustained till the end of the measurements in Group II. In Group I the fall sustained till the 24th hour, but from this point there was not

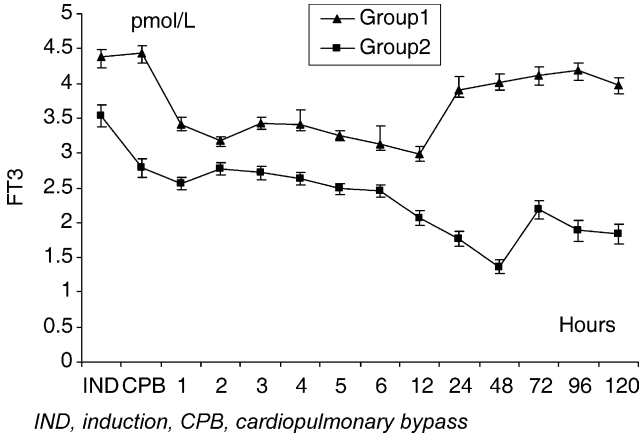


Fig. 2. Time course of the serum concentrations of the free T_3.

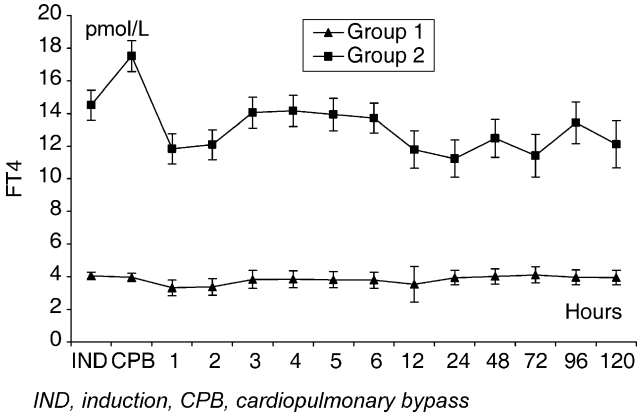


Fig. 3. Time course of the serum concentrations of the free T_4.

any significant difference in the levels in regard to the baseline values ($P>0.05$). The mean fall of fT_3 between the groups was statistically significant from the 2nd hour till the end of the study ($P<0.001$) (Fig. 2).

3.4. Plasma free T_4 levels

The fT_4 level was significantly lower in the T3 group because of the TSH lowering effect of T3 depleted fT4 in the T3 group ($P<0.001$). After the initiation of CPB, there were significant falls in T4 levels in both groups which were sustained for 3 h ($P<0.001$). After the 6th hour, again, a significant decline was observed in the control group, while there were no further significant changes throughout the remainder of the study in the T3 group (Fig. 3).

3.5. Hemodynamic effects

Before induction of anesthesia, the T_3 and study group were not significantly different with respect to some of the hemodynamic parameters (pulmonary artery pressure, pulmonary and systemic vascular resistance) ($P>0.05$) whereas cardiac index ($P<0.001$), pulmonary capillary wedge pressure (PCWP; $P<0.05$), central venous pressure (CVP; $P<0.01$) and Systemic venous oxygen saturation (SVO2) ($P<0.05$) was significantly higher in the T3 treated group. These parameters were evaluated subsequently every 4 h till the 24th hour (Table 2).

3.6. Cardiac index

Cardiac index remained higher in all subsequent time points in the T3 group ($P<0.01$).

3.7. Systemic vascular resistance (SVR)

Although the SVR levels were similar in the preoperative period in both groups ($P>0.05$), the levels remained lower in T3 group after the 12th hour ($P<0.001$).

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Table 2
Hemodynamic responses in both groups

	CI (l/s/m^2)			SVR (dyn/s/m^2)			PVR (dyn s cm^{-5})			MPAP (mmHg)		
	Group I	Group II	*P*	Group I	Group II	*P*	Group I	Group II	*P*	Group I	Group II	*P*
Before sternotomy	1.6±0.3	1.5±0.1	0.020	2207±455	2081±246	0.12	280.4±71.5	270±44.4	0.42	24.1±4.8	22.5±4.2	0.13
4th hour	1.8±0.4	1.6±0.2	0.006	1979±389	1981±250	0.98	266.3±86.5	260±43.5	0.68	21.1±5.2	20.8±4.0	0.77
8th hour	2.0±0.4	1.7±0.2	0.002	1899±350	1908±249	0.88	242.4±68.8	249±43.9	0.57	17.4±6.3	17.8±4.0	0.84
12th hour	2.1±0.4	1.8±0.2	0.001	1716±333	1866±243	0.024	210.1±53.4	238±44.1	0.09	17.6±4.7	18.2±4.1	0.72
16th hour	2.2±0.3	1.9±0.1	0.001	1680±335	1797±230	0.07	190.4±52.1	230±45.3	0.001	17.8±4.5	18.3±3.6	0.28
20th hour	2.3±0.3	1.9±0.1	0.001	1586±305	1696±228	0.07	172.3±51.5	222±46.3	0.001	17.4±4.0	18.5±3.3	0.26
24th hour	2.4±0.3	2.0±0.1	0.001	1382±279	1502±230	0.039	155.4±49.4	208±45.7	0.001	17.5±4.3	19.1±3.1	0.24
	PCWP (mmHg)			CVP			SvO2			Heart rate		
	Group I	Group II	*P*	Group I	Group II	*P*	Group I	Group II	*P*	Group I	Group II	*P*
Before sternotomy	13.9±4.9	11.9±2.3	0.002	9.6±2.7	7.8±2.0	0.002	44.9±5.5	42.6±4.3	0.03	69.3±10.2	71.4±13.1	0.44
4th hour	11.4±3.3	10.2±2.0	0.056	7.3±2.8	6.8±1.7	0.42	51.8±5.8	45.1±4.1	0.001	78.4±13.2	82.4±16.2	0.22
8th hour	9.4±2.6	9.5±1.8	0.81	6.5±1.9	6.0±1.5	0.18	54.6±4.7	47.3±4.2	0.001	82.3±15.1	83.3±16.4	0.77
12th hour	9.9±2.9	10.1±1.6	0.67	6.7±1.4	6.1±1.3	0.06	57.1±7.4	49.0±4.3	0.001	95.4±14.3	94.1±11.1	0.72
16th hour	10.3±2.9	10.1±1.2	0.58	6.7±2.0	6.4±1.0	0.34	61.2±4.3	49.0±3.8	0.001	96.2±16.2	93.4±14.4	0.37
20th hour	8.9±3.0	9.0±1.1	0.81	6.2±1.4	6.4±1.0	0.65	62.4±4.0	48.5±3.0	0.001	98.4±14.4	96.3±15.4	0.54
24th hour	8.0±2.8	8.6±1.0	0.24	5.9±1.3	5.9±1.0	0.78	62.8±3.3	49.5±3.7	0.001	97.3±12.2	97.3±11.4	1.00

CI, cardiac index; SVR, systemic vascular resistance; PVR, pulmonary vascular resistance; MPAP, mean pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; CVP, central venous pressure; SvO2, venous O2 saturation.

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3.8. Pulmonary vascular resistance (PVR)

As stated in SVR, the similar preoperative levels ($P>0.05$) of PVR in both groups were remained lower in the T3 group after the 12th hour ($P<0.05$).

3.9. Mean pulmonary artery pressure (MPAP)

The similarity of the MPAP levels between the two groups were conserved throughout the study period ($P>0.05$) except the 24th hour where the levels were significantly lower in the T3 group ($P<0.05$).

3.10. Pulmonary capillary wedge pressure (PCWP)

Although the preoperative PCWP levels were significantly higher in the T3 group ($P<0.05$), the levels remained similar in the rest of the study ($P>0.05$).

3.11. Central venous pressure (CVP)

Like PCWP levels the higher preoperative CVP levels of T3 group ($P<0.01$) remained similar after the operation with the control group ($P>0.05$).

3.12. Systemic venous oxygen saturation (SVO2)

The preoperatively higher levels of SVO2 of the T3 group remained higher than the control group in all study periods ($P<0.001$).

3.13. Inotropic requirements

Although in both groups the patients were weaned off bypass with similar doses of inotropes, the mean inotrope doses of the groups showed significant differences in the first postoperative 24 h in the ICU. In T3 treated group the mean dobutamine dose was 5 ± 1.2 μg/kg/h whereas it was 8 ± 1.1 μg/kg/h in the control group in the 24th hour ($P<0.001$). The dopamine dose of the T3 group was 3 ± 0.1 μg/kg/h, whereas it was 6 ± 2.1 μg/kg/h in the control group ($P<0.001$).

In the T3 group IABP was inserted in 8 patients in weaning from the CPB or in the intensive care unit (ICU) because of myocardial failure where as IABP was inserted in 17 patients for the same reasons in the control group ($P<0.05$) (Table 3).

3.14. Clinical outcome measures (mortality and morbidity)

There was no difference between two groups in incidence of myocardial infarction, postoperative mechanical ventilation and the incidence of pre- and postoperative complications. Only duration of ICU stay was significantly shorter in the T3 group ($P<0.001$).

Table 3
Postoperative morbidity and mortality in T_3 and placebo groups

	T_3 (Group I)	Placebo (Group II)	P
Myocardial ischemia	3	7	0.17
Myocardial infarction	3	5	0.71
Atrial fibrillation	5	5	1.00
IABP	8	17	0.03
Death	3	3	1.00
Stay of ICU (day)	2.3 ± 0.9	3.4 ± 0.8	<0.001

IABP, Intra-aortic balloon pump; ICU, intensive care unit.

4. Comment

Previous studies have demonstrated the beneficial effects of treatment with T_3 in the setting of LV dysfunction as well as after systemic hypothermia with extracorporeal circulation [4,5]. Novitzky and colleagues examined the effects of administration of T_3 at the termination of CPB in patients with preexisting LV dysfunction and reported a reduced inotropic requirement. Dyke and associates [6] using an isolated rabbit heart model, found that T_3 treatment administered immediately at the time of reperfusion restored peak developed pressure after ischemia.

Thyroid hormone has profound effects on the heart and cardiovascular system [1,2]. Although the sequale of chronic hyperthyroid and hypothyroid states are well documented, the effects of acute alterations in serum hormone levels have also been characterized. CPB results in a ‘euthyroid sick’ state [8,9], and interest has focused on the relationship between low serum triiodothyronine (T_3) levels and postoperative cardiovascular hemodynamics. Accumulating experimental data suggest that pharmacologic T_3 supplementation may improve hemodynamic parameters after ischemic injury in animal models of CPB [10,11] and isolated heart studies [5,6]. Limited clinical data also suggest the benefit of short term T_3 supplementation in the peri-CPB period [12,13].

The study of Walker and Crawford [14] demonstrated that pretreatment with T_3 in cardiomyopathic myocytes preserved β-adrenergic responsiveness after hypothermic cardioplegic arrest and rewarming. They concluded that their finding has particular clinical relevance in that preemptive treatment with T_3 might be a useful therapeutic adjunct by preserving responsiveness to conventional β-adrenergic agonist therapy in the setting of chronic LV dysfunction and after cardioplegic arrest.

Thyroid hormone deficiency can alter cardiac muscle function by decreasing the activity of several enzymes involved in the regulation of myocyte calcium fluxes [15] and the expression of several contractile proteins [16]. Cardiac muscle functional changes, such as alterations in calcium uptake and release jointly leading to depressed inotropism [17], have been documented to occur in hypothyroid animals.

There are numerous studies on the intravenous use of the thyroid hormone in heart surgery for its inotropic effects, but the oral use for this purpose is highly limited

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[18]. In the lights of the aforementioned studies, we aimed to study the effects of oral pretreatment with T_3 in patients with impaired LV functions and undergoing CABG. The use of thyroid hormones (especially T_3 form) for obesity in normothyroid patients in doses of 125–250 μg/day with only mild symptoms and signs of thyrotoxicosis induced to use it in safety [19]. We did not correct the thyroid measurements for hemodilution, but the dose of T3 seemed to maintain a normal fT3 in plasma especially in the peroperative period in the treatment group compared to the control group. We found striking results such as better myocardial function after the operation (the difference of cardiac index between these two groups reached a significant level while the difference of the SVR was not statistically significant in our study) and lesser requirements of inotropic agents in patients treated with T_3 preoperatively.

In our study, oral T3 improved postoperative cardiovascular performance and resulted in decreased inotropic requirement. As an expected finding SVR showed a significant decline in T3 group after the 4th hour. Because there was not a significant reduction in PCWP in T3 treated patients compared with the placebo group the fall of SVR could be caused by the improved cardiac output. The hemodynamic advantage of afterload reduction appears to outweight the disadvantages of increased cardiac output and work. As a measure of cardiac output and peripheral perfusion the MVO2 measurements showed the benefits of T3 in the study group. All these are the advantages can be explained by the known affects of thyroid hormone to increase cardiac contractility and to lower SVR.

In this study oral T3 treatment was achieved safely without any untoward changes in blood pressure, heart rate or cardiac rhythm. We did not observe adverse cardiovascular affects such as anginal symptoms and supraventricular arrhythmias. And in contrary to the study of Klemperer et al. [20] atrial fibrillation rate was same in both groups.

Also there was not any difference between the two groups in the incidence of myocardial ischemia, myocardial infarction and death. But, the duration of the length of stay in ICU was significantly less in the T3 group.

In conclusion, the low T3 state resulting from CPB can be safely reversed by the oral T3 administration to the patients with impaired left ventricular function undergoing CABG. It enhances early postoperative hemodynamic performance and a reduction in pharmacologic support requirements has been demonstrated. Therefore in such patient groups, in addition to the usual inotropic support, it can be used to maximize the metabolic support for the reduction of high risk for poor postoperative prognosis. However, our study lacks the precise timing for the pretreatment. We started the oral form one week before the operation. Whether this time should be prolonged or shortened must be further inspected.

References

[1] Klein I. Thyroid hormone and the cardiovascular system. Am J Med 1990;88:631–7.

[2] Polikar R, Burger AR, Scherrer U, Nicod P. The thyroid and the heart. Circulation 1993;87:1435–41.

[3] Hamilton MA. Prevalance and clinical implications of abnormal thyroid hormone metabolism in advanced heart failure. Ann Thorac Surg 1993;56:S48–S53.

[4] Novitzky D, Human PA, Cooper DK. Inotropic effect of triiyodathyronine following myocardial ischemia and cardiopulmonary bypass: an experimental study in pigs. Ann Thorac Surg 1988;45:50–5.

[5] Holland FW, Brown PS, Clark RE. Acute severe postischemic myocardial depression reversed by triiyodothyronine. Ann Thorac Surg 1992;54:301–5.

[6] Dyke CM, Yeh Jr T, Lehman JD, Abd-Elfattah A, Ding M, Wechsler AS, Salter DR. Triiyodothyronine-enhanced left ventricular function after ischemic injury. Ann Thorac Surg 1991;52:14–19.

[7] John Castellan Jr N. In: Nonparametric Statistics for the Behavioral Sciences Sidney Siegel. New York: McGraw-Hill; 1988, p. 174–83 chapter 7, section 7.2.

[8] Holland FW, Brown PS, Weintraub BD, Clark RE. Cardiopulmonary bypass and thyroid function: a "euthyroid sick syndrome". Ann Thorac Surg 1991;52:46–50.

[9] Robuschi G, Medici D, Fesani F, Barboso G, Montermini M, d'Amato L, Gardini E, Borciani E, Dall'Aglio E, Salvi M. Cardiopulmonary bypass: 'a low T_4 and T_3 syndrome' with blunted thyrotropin (TSH) response to thyrotropic-releasing hormone (TRH). Horm Res 1986;23:151–8.

[10] Novitzky D, Matthews N, Shawley D, Cooper DK, Zuhdi N. Triiyodothyronine in the recovery of the stunned myocardium in dogs. Ann Thorac Surg 1991;51:10–17.

[11] Dyke CM, Ding M, Abd-Elfattah AS, Loesser K, Dignan RJ, Wechsler AS, Salter DR. Effects of triiyodothyronine supplementation after myocardial ischemia. Ann Thorac Surg 1993;56:215–22.

[12] Novitzky D, Cooper DK, Barton CI, Greer A, Chaffin J, Grim J, Zuhdi N. Triiyodothyronine as an inotropic agent after open heart surgery. J Thorac Cardiovasc Surg 1989;98:972–8.

[13] Novitzky D, Cooper DKC, Swanepoel A. Inotropic effect of triiyodothyronine (T_3) in low cardiac output following cardioplegic arrest and cardiopulmonary bypass: initial experience in patients undergoing open heart surgery. Eur J Cardiothorac Surg 1989;3:140–5.

[14] Walker JD, Crawford Jr FA, Spinale FG. 3,5,3′ Triiyodothyronine-L-Thyronine pretreatment with cardioplegic arrest and chronic left ventricular dysfunction. Ann Thorac Surg 1995;60:292–9.

[15] Dillmann WH. Biochemical basis of thyroid hormone action in the heart. Am J Med 1990;(88):626–32.

[16] Ojamaa K, Klein I. In vivo regulation of recombinant cardiac myosin heavy chain gene expression by thyroid hormone. Endocrinology 1993;132:1002–10.

[17] Rohrer D, Dillmann WH. Thyroid hormone markedly increases the mRNA coding for sarcoplasmatic reticulum Ca^{2+}-ATPase in rat heart. J Biol Chem 1988;263:6941–4.

[18] Murai N, Katayama Y, Yamada T, Imazeki T, Irie Y, Kiyama H, Sato Y, Hata I, Yoshida H, Mukouyama M. Thyroid hormone and myocardial metabolism after heart surgery in dogs. Asian Cardiovasc Thorac Ann 1999;7:13–17.

[19] Bruy GA, Melvin KW, Chopra IJ. Effect of triiodothyronine on some metabolic responses of obese patients. Am Clin Nutr 1973;26:715–21.

[20] Klemperer JD, Klein IL, Ojamaa K, Helm RE, Gomez M, Isom OW, Krieger KH. Triiodothyronine therapy lowers the incidence of atrial fibrillation after cardiac operations. Ann Thorac Surg 1996;61(5):1323–7.

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