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Splenectomy may have more complications than currently proven

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ABSTRACT

The spleen has been one of the least understood major organs for centuries. Its significance is relatively well-known today but it seems that all aspects of its activities are not fully understood. Persian medicine (PM) has special views on the function of spleen; many side effects were reported in PM due to spleen dysfunction. On the other hand nowadays splenectomy as a treatment strategy is recommended for some disorders and increasing risk of infections is considered as the most important long term side effect of that. In this study, we hypothesize that splenectomy may have more side effects than currently proven.

According to PM, spleen is in close connection with liver, cardiovascular system, stomach, bone, brain and skin, and that is why any kind of spleen dysfunction leads to change in blood viscosity, appetite and bone strength, liver dysfunction, mood and skin disorders, cancer formation and fever. Considering this viewpoint it can be hypothesized such side effects may also occur after splenectomy.

Proven complications of splenectomy include hypercoagulated state, cardiovascular events and infectious diseases but there is also some evidence about increased risk of cancer, skin disease like systemic lupus erythematosus, mood disorder such as depression, defective bone formation and impairment of immunity which can be considered as different levels of evidence to confirm the hypothesis.

But for some others such as changes in appetite, there are no studies let alone convincing evidence. Future research about theses possible complications may lead to novel results.

Introduction

The spleen is known as a large part of reticuloendothelial system which is composed of an encapsulated mass of vascular and lymphoid tissue [1]. The main role of spleen in regulating the immune system as well as influencing metabolic and endocrine functions has just become clear over the past few decades, so for many centuries, the spleen has been the least understood and the most mysterious major organ [2].

The main known spleen activities include removing and enmeshing senescent and defective RBCs to keep a healthy quality of blood, acting as an extra medullary site for hematopoiesis [1,2], recycling iron [2], antibodies synthesis in white pulp [1,2], expelling antibody-coated bacteria and antibody-coated blood cells from the circulation, acting as a major source of properdinan which is an important protein in the body's response to certain kinds of infection [1].

Even with the recognition of spleen activities it has always been thought-out as an obscure organ that is possible to live without [3]. Nowadays splenectomy as a treatment strategy is recommended for some disorders and increasing risk of infections is considered as the most important long term side effects of that [1,2,4]. But in some traditional system of medicine such as Persian medicine (PM) which

formed on Iran's plateau more than thousands years ago [5], there was a different view about spleen and its dysfunction [6]. Due to approving many of their theories in new research, the evaluation of others can be considered worthwhile [7–9].

Background of hypothesis

Spleen in Persian medicine

The spleen has been defined as a tongue-shape, dark purple-colored porous organ that is located in the upper left side of the stomach and protected by the rib cage [6]. It is covered by a membrane which is in contact with diaphragm and the other abdominal viscera [6,10]. The spleen has close relationship with liver through vessels between them and probably via *Engheras* (Pancreas) that is named as a spleen neck in some PM textbooks [11]. It is also considered in relationship with stomach via arteries and veins that located between them [12,13]. Spleen anatomy which was described in PM, regardless of physiology and their relationship, is similar to today's anatomy and indeed, what was introduced as a communication link between the spleen and the liver is the splenic vein [10]. According to conventional anatomy, the

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hepatic portal vein is formed by the union of the splenic veins and the superior mesenteric behind the neck of the pancreas [14] Also, the connections between spleen with stomach and pancreas in PM match with location of gastrosplenic and splenopancreatic ligaments and their vessels [14].

Avicenna, the most famous Persian physician and philosopher [15], same as Hippocrates was at this credence that the human body partly consists of four humors [16]. In his masterpiece, called "Qanon of Medicine", Avicenna has described spleen or "Tahal" as an organ specialized to store black bile –one of the humors- and regulates its secretion into the blood circulation [17]. So one of the most important roles of spleen is to prevent the entry of high amounts of black bile into the blood circulation [18] and also to refine (as purificator) excess black bile from blood circulation. It also makes some changes in the black bile produced in the liver [6]. Some Persian physicians believed that the spleen through the pancreas absorbed black bile from the liver [13].

Avicenna described that normal black bile is responsible for blood viscosity and also essential for nutrition and preservation of some organs such as bones and spleen itself [6].

He also mentioned the different types of abnormal black bile which are produced in special conditions and lead to various diseases [6]. Furthermore, many physicians of PM believed that there is a special correlation between spleen and other system and organs [9–13].

Probable side effects of spleen dysfunction and spelenectomy according to PM

According to PM, health of many organs such as heart, liver, stomach, skin, brain, nervous system and bone depends on having healthy spleen. Diseases caused by spleen disorders are listed in Table 1. Patients with some kind of sick spleen will be more prone to these kind of diseases if they eat some kind of food with the ability to produce black bile especially the abnormal type of it and have a sedentary life without any black bile purification [13]. Weakness of spleen is considered more dangerous among women, children and cold temperament people [6].

One of the important side effects of spleen dysfunction is increased risk of cancer due to disruptions in the nature or amount of black bile because some kind of black bile considered as the feeder of cancerous tissue in PM [6,19].

 Table 1

 Complications spleen dysfunction according to PM aspects.

Affected organ	Complications
Skin disorder	Vitiligo [6,12]
	Brown spots(a kind of hyperpigmentation) [6,12,19–24]
	Freckles (a kind of hyperpigmentation) [23,25]
	Psoriasis [6,12,19-21,23,24]
	Skin color Changing [12,22,25,26]
	Skin itch [22,23]
	Melasma [21]
	Malignant ulcers [22,23]
Digestive system	↑ or ↓ Appetite [22]
	Heart burn [26]
Psychological	Dillusion [6,12,19–21,23,26,27]
disorder	Grief and depression [6,12,19-21,23,26,27]
	Melancholia [6,12,19-21,23,26,27]
	Fear and anxiety [6,12,19-21,23,26,27]
Vascular dysfunctions	Varicose vein [6,12,19,21,23,24]
	Hemorrhoid [12,21,25,28]
	Elephantiasis [6,12,22,24]
	Lower limb vascular dilation Could be pertaining to DVT
	[12,19,21,23]
Liver dis.	Decrease and decay in liver function [21]
Hematologic dis.	Blood decadence (↓Blood quality, ↑blood density),
	Anemia, Leukemia, Septicemia, Thrombosis [21,24,27]
Infectious dis.	Fever [23]
Malignancy	Cancer [6,19,23,24]

Proven side effects of splenectomy

Nowadays increased risk of infection is considered as the most important long-term complication of splenectomy [4]. Cardiovascular and hematologic disorders also are accepted as one of the main side effects. Although it is believed that the absence of spleen has minimal long-term effects on the hematologic profile [1], there are compelling and sufficient evidences for a hypercoagulated state after splenectomy [29].

Follow up of 140 splenectomized patients with primary immune thrombocytopenic purpura in one Case-Control Study indicated an increased risk of thromboembolic and cardiovascular events [30]. The risk of portal vein thrombosis may reach 40% for patients presenting with both splenomegaly and myeloproliferative disorders [2].

Researchers also discovered high death rate due to pulmonary embolism and coronary artery disease in splenectomized patients in a 27-year follow-up [31]. Another study showed that mortality rate because of ischemic heart disease was 1.9 times more than others in splenectomized patients [29]. Also 5.6 fold increased rate of arteriosclerotic events including stroke, myocardial infarction, and coronary or carotid artery surgery was shown in splenectomized persons (who had hyposplenism) compared with hyposplenic patients who had not had splenectomy [29]. Spleen sends monocytes to the injured heart tissue (to participate in wound healing) and this is effective in the reconstruction of the heart after myocardial infarction [32].

On the other hand some findings showed that splenectomy increased the atrial fibrillation 4 weeks after surgery because the IL-10 which is derived from spleen has been depleted and it led to inflammatory fibrosis in atrial tissue [33].

Hypothesis

In this study, using the view point of PM about complications of spleen dysfunction and considering the existing sufficient evidence for some of them, we hypothesize that splenectomy may have more side effects than currently proven because spleen may have more functions than what is imagined. According to our hypothesis risk of cancer, hemorrhoids, skin diseases, mood disorders such as depression, defective bone formation and changes in appetite and digestive system may increase after splenectomy.

Evaluation of the hypothesis; new evidence about probable complications of splenectomy

Cancer

Risk factors of cancers have always been an important topic. A significant increase of malignant tumor induction has been reported in splenectomized rats and mice [34]. On the other hand some epidemiological studies showed an association between splenectomy and increased risk of developing cancer [31,35]. In a cohort for 27-year follow-up of 8149 cancer free splenectomized patients, 13% of them were diagnosed with cancer during the follow-up. Results showed an increased risk for certain solid tumors in mouth, esophagus, liver, colon, pancreas, lung and prostate with rate ratio of 1.3–1.9, and hematologic malignancies like non-Hodgkin lymphoma, Hodgkin lymphoma, multiple myeloma, acute myeloid leukemia and any leukemia with rate ratio = 1.8–6. They also showed an increased risk of death due to any cancer include liver, pancrease and lung cancer, lymphoma and any leukemia with rate ratio of 1.3–4.7 [31].

Another study also showed an increased risk for some specific cancer sites among 5212 splenectomized patients [31]. A non-significant 40% increased risk of total cancer and significant increased risk of ovarian and lung cancers was also shown in another study with average follow-up of 9 years in 984 cancer free splenectomized patients [31].

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