Short Communication

The Future of Thyroid Surgery

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During my recent visit to South Korea, my Korean colleague informed me, with obvious displeasure, that incidence of surgery for thyroid cancer in his country had decreased by 40% in recent years. My response to this information seemed to puzzle him but we went on to talk about other topics and he did not press any further. I would like to take this opportunity to elaborate on what I meant and what I believe about the future of thyroid surgery.

Let me first accept the consensus that invasive surgery as a whole is in a slow but inevitable decline. Many diseases are being discovered earlier than ever, making prevention and early intervention increasingly viable. Endoscopic and other minimal invasive therapies are seeing ever broader application. Conventional invasive surgeries will eventually be applied to narrower indications. But the current dip in thyroid cancer surgery does not indicate a bleak future for thyroid surgery in general because thyroid surgery had always been through ups and downs and the recent decline is just another fluctuation in its history.

This is not the first time that bleak prognosis had been declared for thyroid surgery. As early as 1866, Samuel Gross, the 12th president of the American Medical Association and one of the founders of the American Surgical Association, wrote (1):

“If a surgeon should be so adventurous or foolhardy as to undertake thyroidectomy, every step he takes will be environed with difficulties, every stroke of his knife will be followed by a torrent of blood, and lucky will it be for him if his victim lives long enough to enable him to finish his horrid butchery ... no honest and sensible surgeon, it seems to me, would ever engage in it.”

Eventually when techniques improved, and Kocher reported a mortality rate of 0.5%, the pendulum swung in the opposite direction. A large number of patients underwent thyroidectomy for benign goiter out of cosmetic concerns in the absence of distressing symptoms. This led to a large number of patients suffering from post-surgical hypothyroidism and Kocher lamented, “Removal of the thyroid gland has deprived my patients of what gives them human value. I have doomed people with goiter, otherwise healthy, to a vegetative existence. Many of them I have turned to cretins, saved for a life not worth living.”

At this point, what was once “horrid butchery” had become a relatively safe procedure, a great medical triumph, but was over-applied. An international committee led by William Ord concluded that what Kocher termed “cachexia strumi priva” was in fact induced by the loss of thyroid function, and eventually oral ingestion of desiccated thyroid was used to relieve the symptoms. After that, thyroid surgery was on a rise again and in 1927, the number

of annual thyroidectomies in the Cleveland Clinic surpassed 2,500. But later, with the introduction of iodized tap water and iodized salt which significantly decreased the incidence of endemic goiter, the invention of thiouracil and radioiodine therapy for Graves' disease, a marked drop in the use of external radiation in the treatment of tonsillitis and acne, and the introduction of better diagnostic tools such as core needle biopsy, all conspired to decrease the need for thyroid surgery. The number of thyroidectomies in the Cleveland Clinic in the late 1960's fell to 50 cases per year (2). The situation was similar in many institutions, which lead some doctors to declare that thyroid surgery will eventually become unimportant. But as newer diagnostic tools improved, more thyroid tumors were discovered and thyroidectomies increased. Amid hugely increased incidence of thyroid surgery, in 2003, Ito et al. (3) published their findings regarding the active surveillance of papillary microcarcinoma, which proposed that if patients with proven papillary carcinoma of the thyroid less than 10 mm in size were not given surgery but were put on observation, not more than 15% of tumors would show significant signs of growth after 10 years. Thyroid cancer surgery still continued to increase until after the release of epidemiological studies by Davies and Welch (4) which concluded that the increased application of surgery had no effect on the total mortality from thyroid cancer, after which we witnessed the current decline in thyroid cancer surgery.

The history of thyroid surgery, in fact any surgery, is a pendulum between overzealousness leading to over-treatment followed by a backlash and a marked decrease of cases. It is the basic nature of medicine to veer between optimism and caution. What we are witnessing in South Korea and elsewhere today is not a step backwards or the beginning of the end for thyroid surgery, but an inevitable stepping stone in the march for progress.

When the thyroid is removed, a replacement of thyroxine is all that is needed to preserve the general health of almost all patients, therefore we have remained blind to unseen functions that the thyroid may have. We know that the only essential hormones the thyroid produces is thyroxine and its derivatives. We also know that the thyroid produces a vast array of proteins whose functions are largely unknown. We know that calcitonin can suppress the level of serum calcium, but we do not supplement calcitonin after thyroidectomy because humans can survive without it. The same probably applies to most other hormones produced by the thyroid. But what if some unknown, and usually unnecessary, hormone is overproduced? Could this not be a cause of a disease?

I have reported 2 cases of spontaneous remissions from anorexia nervosa after thyroidectomy (5). After publication, I learned that some of my colleagues have experienced similar cases. This phenomena remains unexplained. However, Tavares et al have reported that an infusion of amino-procalcitonin, produced by the thyroid, into the third ventricle of the rat brain resulted in inhibition of food intake and stimulated hypothalamic appetite control (6). Perhaps some variants of anorexia nervosa are caused by the hyper-secretion of amino-procalcitonin. If a subtype of anorexia nervosa is actually the result of endocrine hyperfunction, thyroidectomy could be a possible treatment.

More importantly, however, those of us who see thyroidectomized patients on a daily bases have noticed that we see fewer cases of senile dementia in patients thyroidectomized at a younger age. Much has been discussed about the effect of conventional thyroid hormones on Alzheimer's disease (7). However, previously uninvestigated thyroid-derived proteins have also recently been implicated in the development of Alzheimer's disease (8). Although the observation is so far experimental, South Korea, with so many thyroidectomized patients, is

in a unique position to perform a prospective clinical study. If thyroidectomy is proven to be a significant deterrent for senile dementia, this could open new opportunities for future study.

In most developed countries today, we have become so efficient at detecting and treating cancer that if all cancers disappeared from existence, life expectancy of the total population will increase by only a few years. Most cancers are gradually becoming, if not curable, manageable. The most pressing First World medical problems are eating disorders (including obesity and its co-morbidities), senile dementia, sarcopenia, and osteoporosis. There are currently no effective cures for these diseases and none of them are projected to decrease in the foreseeable future. The last three are particularly related to the aging population. If senior citizens were freed from dementia, sarcopenia, and osteoporosis, the burden of nursing and caring for the aging population will be greatly diminished. The impact on the cost of medical care is immeasurable. As I have already elaborated above, eating disorders and dementia may be related to the thyroid. Muscle and bone metabolism have long been known to be associated with the thyroid (9,10).

There may be more benefits to thyroidectomy than we are currently aware of. Conversely, there could be drawbacks to thyroidectomy that we are currently unaware of. Some thyroidectomized patients, particularly in North America, have reported chronic fatigue on synthetic levothyroxine, even with thyroid stimulating hormone (TSH) in the normal range, which was alleviated when they switched to desiccated thyroid. Patients like Janie Bowthorpe, in typical American fashion, started their own patient organization to promote the usage of desiccated thyroid (11). Meanwhile, in Japan, where partial or subtotal thyroidectomy has long been the norm, the demand for desiccated thyroid is so low that production was ceased in 2014. Desiccated thyroid contains substances other than thyroxine that are absent in synthetic drugs. I would like to suggest the phrase “post-thyroidectomy lethargia” to describe this symptom of fatigue and loss of concentration among total thyroidectomy patients on synthetic thyroxine with adequately controlled TSH. The phenomenon suggests that there are active substances other than thyroxine produced by the thyroid which are necessary for some patients. Perhaps such substances can be substituted by dormant hormones produced elsewhere in the body, and some patients may have a congenital deficit of such substitutes. Alternately, the thyroid may be producing substitutes for congenitally absent hormones, and the defect only becomes dominant after total thyroidectomy.

Shinichi Fukuoka, currently of Aoyama Gakuin University, has observed that in some kinds of knockout mice, the expected loss of function may not materialize because physiological redundancies will activate to fill the void. He called this a biological “dynamic equilibrium” and based his ideas on the concept of “dynamic state” proposed by Rudolf Schoenheimer (12). I took this a step further and presented the concept of “vestigial endocrinology” at the plenary lecture of the annual meeting of the Korean Thyroid Association in 2012. The idea is that a vast array of hormones in our bodies are inactive evolutionary vestiges waiting in the sidelines for an opportunity to become dominant. As we age, and the major players of the endocrine system lose their efficacy, more and more side characters become active trying to fill the vacant void. These vestigial hormones were never meant to perform the functions they substitute for as a primary objective, thus having the potential to present collateral effects. The thyroid may be one of the centers of this vestigial endocrine action.

There is more to thyroid surgery than the removal of tumors. The name “endocrine surgery” suggests that this is the art of controlling hormones through surgery. That is an infinitely more sophisticated endeavor than the removal of a tumor.

Granted, this is mostly conjecture, and conjectures can be dangerous things. Unrelated to surgery but currently topical, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus is presently spreading around the world. Some epidemiologists have noted that the rate of death from coronavirus disease 2019 (COVID-19) in Taiwan, South Korea, and Japan is lower than elsewhere and conjectured that mandatory Bacille Calmette-Guérin vaccinations, which are instituted in this area, might offer protection from the virus. Of course, epidemiologists would focus on tuberculosis and the effect of vaccinations. As a thyroid specialist, I noted that these were the countries with the highest consumption of dietary seaweed, and hence high iodine intake. What sounds like a viable theory could be just a reflection of our focus. Although there have been reports in animals (13) and in vitro experiments (14) that iodine stifles virus activity, while both Lugol's solution and Lecithin-bound iodine were used as remedies for pulmonary symptoms for over a century combined, there is no solid evidence that iodine suppresses viral infections. We must all be aware of how much we are biased by our areas of expertise. When your only tool is a hammer, all of your problems tend to look like nails. With that caveat, I conjecture that thyroid surgery potentially has wider applications than is currently considered.

Contrary to common belief, surgical thyroid intervention is still a relatively young procedure. In 1937, a magnificent airship called the Hindenburg exploded in a fiery accident over an airfield in New Jersey. This was a major setback in the history of aviation and many voices lamented the end of air travel. The Hindenburg disaster was 154 years after the first manned balloon flight. We, in 2020, are only 154 years removed from Samuel Gross and "horrid butchery". If we can expect aircraft to evolve, so too can we expect thyroid surgery to evolve. And we still have a great deal of distance to go.

The death of thyroid surgery has been declared before. It will be declared again in the future. We are still facing a vast void of unexplored knowledge, compared to which our present existing knowledge is meager and primitive. And knowledge can only be gained by marching forward.

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