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EDITORIAL

The dilemma of papillary thyroid microcarcinoma management. To operate or not to operate, that is the question

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The trolley problem is a classic moral dilemma. A runaway trolley is racing down a hill toward five tied-up people on the tracks. You are standing next to a lever that controls a switch that could divert the trolley onto a sidetrack and save the five people. However, there is a single person tied up on that sidetrack. Should you pull the lever? It is OK to sacrifice one in order to save five? It is only natural that this dilemma should come to mind when considering the proper course of treatment for papillary thyroid microcarcinoma (mPTC).

We know that mPTC is almost always an indolent disease (actually it is an unexpected finding in 22% - 35% of non-thyroid related death autopsies). We know that only about 1% of mPTC will behave aggressively. Furthermore, we realize that we overtreat these patients even though our main therapy of choice, surgery, is far from risk free [1]. Thus, let us restate the trolley problem this way: a sinister surgeon (with sharp scalpel in hand!) looks for 100 mPTC patients with the wicked intention of depriving them of their source of thyroid hormone (may surgeons forgive me!). We can safeguard the vast majority of these terrified patients by simply not sending them to the surgeon's office. But, sadly, such a decision would mean that one of those 100 patients will eventually develop metastatic disease in the future. Is that acceptable? Is it reasonable to sacrifice 99 to save 1? If truth be told, today we have the weaponry to beat mPTC in almost all cases. Hence, the crux to the entire dilemma described above is diagnostic precision [2]. The real challenge is no longer how to cure mPTC but rather how to identify the 1% of patients with the aggressive disease. In this context it is understandable that some experts argue in favour of referring to mPTC as *papillary microtumor*, thus avoiding use of the emotionally charged word *cancer* [3]. This practice has been successfully tested in Australia with excellent results among patients [4].

In 1993, the low aggressiveness of mPTC led surgeons at the Kuma Hospital (Kobe, Japan) to initiate an active surveillance (AS) trial for low risk mPTC as an alternative to surgery [5]. The authors monitored 162 mPTC patients with serial ultrasounds over a period of 8 years. They found that 70% of the tumors remained the same size or even shrank; 10% increased in size more than 10 mm, with only 1.2% generating metastases in the lateral neck lymph nodes compartments. Preliminary data allowed them to recommend what was until then unthinkable: considering AS as a viable alternative to surgery for patients with mPTC. After 25 years practicing AS, Japanese research has revealed that all mPTC patients in whom the disease had advanced during AS were successfully treated by rescue surgery and none died from their disease [6]. In summary, the Japanese experience teaches us that mPTC will advance in only 16% of cases. These will require further treatment in the operating room. This strategy has shown that, in addition to reducing surgical complications, there is no

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increase in morbidity or mortality associated with AS when compared to surgery in the two mPTC cohorts [7].

The Japanese experience became the rule rather than the exception when the measures were integrated into the controversial 2015 ATA Guidelines [8]. However, the AS option has been received with a high degree of scepticism in so-called western countries. The general feeling is that AS on its face is a reasonable treatment path but that the profession needs to proceed with utmost caution. The average endocrinologist, like most everyone, is reluctant to adopt change. My first thought and, perhaps, that of many readers, is to take a wait-and-see approach. But then, I think back to patients who underwent total thyroidectomy because an mPTC who now have poor quality of life due to complications resulting from surgery or replacement therapy with levothyroxine. So, going back to the trolley problem, what do we do with the trolley lever? Just leave it alone and leave fate to the stars? It seems that opinions are gradually changing.

Despite initial hesitation, slowly the super experts are leaning in favour of AS [9]. At the same time they seem to be in a race to go even further. For example, Tuttle et al. raised the bar by recommending AS for PTC tumors up to 1.5 cm (i.e., no longer *micro*). These authors followed almost 300 subjects for an average of more than two years [10]. They observed no metastases (local or distant) and only 3.8% of tumors grew more than 3 mm. Sakai et al. from Japan used AS in cases of PTC up to 2 cm [11]. They have been following 61 PTC (T1b, N0, M0) for more than seven years. Of these, only 7% increased in size and 3% developed local metastases. Their results reiterate the indistinguishability between T1a (pure mPTCs) and T1b tumor outcomes when using AS. Currently there are AS trials ongoing in Canada [12], Australia [13] and Korea [14]. There is no doubt that an eventual paradigm shift will benefit patients (around 99% of those innocent thyroids will be saved!) and costs will be reduced. Taking all the research into account, it seems reasonable for all of us to include AS as the correct initial management path for mPTC.

But amid all the chaos, what are we to proceed? My answer is: individualize and proceed gingerly. We know that those who use AS are correct, but there are other factors that need to be considered, such as personal experience and the environment, both professional and social, in which one works.

It is important to emphasize that AS does not mean the abandonment or alienation of the patient. We need to be convinced that AS is a valid option. Even more, we must be convinced that AS is the *correct* management option. The key is to understand that AS tailors mPTC management to the actual needs of the patient. Once we are convinced that the correct initial treatment option for mPTC is simply to monitor it, everything will run smoother. AS assumes that active surgical treatment is sidelined until the mPTC requires it, i.e., should the tumor begin growing. This approach should bypass the ATA's recommendation not to biopsy infracentimetric nodules.

If we decide to implement AS, we will need to face four challenges.

a) The Multidisciplinary Team will have to endorse the decision to use AS [15].
b) Candidates for AS will have to be carefully screened. The current data classify patients into three categories: ideal, adequate and inadequate. This classification depends on the characteristics of the tumor, the patient and the equipment [16].
c) Endocrinology departments will need to have the capacity to assume a potential increase in workload.
d) And, above all, physicians will have to explain to the patients what they are going to do and why and how it will be done. The patient must accept the challenge and understand the alternatives and risks. It must be made clear to patients that surgical treatment has its drawbacks even in the best of outcomes [17].

While AS may not be the ''be all and end all'', we should consider it another step in our quest to provide the best treatment to a growing number of mPTC patients. While, to date, no molecular marker has proven itself to be adequately reliable in identifying the potentially aggressive mPTC, we can hope that soon such a marker will be found, thus making our trolley dilemma analogy obsolete.

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