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Prostate Cancer-The More We Know, the More We Get Confused?

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The recent release of the clinical results of the Prostate Cancer Intervention vs. Observation Trial (PIVOT) on early prostate cancer [1] and enzalutamide on Castration Refractory Prostate Cancer (CRPC) [2], together with the quality of life analysis of prostate cancer screening by the European Randomized Study of screening for Prostate Cancer (ERSPC) group [3], had added fuel to the hot debate about the optimal management of prostate cancer. In the past few years, there was rapid development in management of various stages of prostate cancer, from chemoprevention, screening, to management of advanced stage disease. However, despite all these new information, it is still uncertain about what is the "best approach" to manage prostate cancer in our daily practice: whether it is a true "fierce tiger" that needs aggressive effort to detect and treat it early to avoid advanced stage diseases or it is just a "little kitten" with which we can live for years peacefully without any need of early intervention.

There was a long publication list of the clinical results of various agents for the management of advanced prostate cancer [2,4-7]. Some of these agents have already approved by FDA for clinical use. Judging from the great interest of doctors and patients on the drugs and the tremendous input from the industry in the development of these products, there was a real and unmet demand in management of advanced prostate cancer. From these studies, the outlook of patients with castration refractory disease after using these drugs was still limited [2,4-6]. Therefore, interest has also been raised in chemoprevention by using 5-alpha reductase inhibitors to prevent development of prostate cancer [8]. Though the best regime for chemoprevention (such as time to start, dosage, and optimal duration, etc.) is still uncertain, it has already aroused great interest of physicians and the public.

Although we know that prostate cancer can progress and is potentially fatal, the role of screening and early treatment is still controversial. The results of the two big trials on prostate cancer not only help us to clear this uncertainty, they just add more confusion to the community [9,10]. The updated thirteen year follow-up data of the Prostate, Lung, Colorectal and Ovarian (PLCO) suggested that there was no evidence of survival benefit for organized annual screening for prostate cancer. However, the latest results of ERSPC reconfirmed their early suggestion that PSA-based screening lead to decrease in prostate cancer specific mortality, though the all-cause mortality remained unchanged. To further complicate the issue, even when a patient was diagnosed to have early prostate cancer, the optimal treatment for that was also controversial. From the results of the Scandinavian Prostate Cancer Group (SPCG-4), radical prostatectomy could significantly reduce the all-cause mortality, prostate cancer specific mortality and risk of metastasis, especially for men younger than 65 years old [11]. However, the results of the PIVOT group, which was thought to be a more representative study for PSA-diagnosed prostate cancer, did not show any significant benefit in all-cause and cancer specific mortality for radical prostatectomy over observation alone [1]. Furthermore, prostate cancer screening may affect the quality of life of patients [3]. The diagnosis of cancer may in fact lead to an immediate increase in incidence of suicide and cardiovascular death, well before the death of prostate cancer itself [12]. Therefore, is it meant that we can do nothing for the condition, but to wait for the occurrence of symptoms?

As urologists, we all saw patients who died of prostate cancer and no doubt it is one of the top cancer death causes in many countries. Also we all would have witnessed the suffering in patients with advanced disease, including bone pain, spinal cord compression, obstructive uropathy etc. Therefore, it will be our duty to try our best to avoid patients entering into these late stages by providing them with early diagnosis and appropriate interventions. The problem for prostate cancer is that it contains a big family of cancers with various types of aggressiveness; from fierce tigers to little kittens. Therefore, risk stratification is important, i.e. identifying those prostate cancer patients who would be more benefited by active treatment and who would be put on observation (or active surveillance). Currently, there are already many systems of risk stratification systems to guide our decision making process [13]. However, we may still need some refinement on the criteria, in particular the possibility of incorporating some molecular markers in the systems to help the improvement in their accuracy. The option of active surveillance should be included in one of the treatment options for early stage prostate cancer, in particular for low risk patients. However, the concept of active surveillance is still not very popular in some clinical practice [14]. While we are still waiting for the final result of ProtecT study, [15] a better education of physician and patients to understand more about the clinical behavior of prostate cancer and also the concept of active surveillance maybe beneficial to some patients when they were diagnosed to have low risk early stage prostate cancer.

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