PERSPECTIVE

Choice of androgen deprivation therapy for prostate cancer

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Keywords: Androgen deprivation therapy; prostate cancer; evidence based medicine; bilateral orchidectomy

The prevalence of prostate cancer [PCa] is rising globally and the rates in Asian countries are expected to increase exponentially [1]. The majority of patients with PCa have metastatic disease at the time of presentation in developing countries [1]. According to National Cancer Control Programme statistics, there have been 1009 new cases of prostate cancer reported in 2019 and is the fifth commonest cancer among Sri Lankan men [2]. The incidence seems to be increasing with the majority presenting with metastatic disease [3, 4]. Medical or surgical [bilateral orchiectomy] androgen deprivation therapy [ADT], is the standard of care for metastatic PCa. ADT is also used as neoadjuvant therapy in patients with locally advanced PCa prior to definitive treatment. Gonadotropin-releasing hormone [GnRH] agonists are the commonly used form of medical ADT especially in the developed world [5]. The reasons given are its reversibility and supposedly better profile of adverse events when compared to surgical ADT. However, a review of published literature in the past 20 years showed that the advantages of medical ADT in terms of sexual dysfunction, osteoporosis, metabolic adverse events and vasomotor symptoms are minimal or inconclusive [Supplementary table 1]. Furthermore, these studies comparing medical versus surgical ADT have not made any conclusive recommendations against surgical treatment.

Compared to surgical treatment, Luteinising Hormone Releasing Hormone [LHRH] agonists achieved significantly lower levels of serum testosterone [6]. However, the clinical significance of such a difference is not clear. The risk of osteoporosis and fracture rate was significantly lower in the bilateral orchiectomy group when compared to LHRH agonists [7]. Teoh et al, showed that the risk of cardiovascular thrombotic events was found to be higher among patients who underwent orchiectomy than LHRH agonists, however, a population-based study from Sweden did not reveal any statistically significant increase in the risk [8, 9].

The survival rates, change in plasma glucose values, risk of cardiovascular disease, cognitive disorders, fracture risk and sexual function after surgical ADT was found to be non-inferior to medical treatment. The popular belief that surgical ADT is associated with poor psychological morbidity and quality of life lacks evidence as studies have shown that the quality of life and sexual function following two treatment modalities were similar [Supplementary table 1- Table S1]. A meta-analysis comparing intermittent vs. continuous ADT did not show any significant difference in overall survival, cancer-specific survival, and progression-free survival but physical and sexual functioning favoured intermittent ADT [10]. The difference in the self-reported quality of life of the participants was also minimal.

Another important factor in selecting the choice of ADT is the cost, more relevant in resource-poor settings. Two studies have compared the relative cost of surgical treatment with LHRH agonist therapy. The cost of orchiectomy was exceeded within 4.2 to 5.3 months and the cost for two years of medical ADT was 10.7 to 13.5 times of surgical ADT. The duration of medical ADT depends on the life expectancy of the patient and in this study, 15% of patients were alive after 10 years [Table S1]. In a study published in 2000, the total cost of bilateral orchiectomy was $2,022 while the cost of treatment with LHRH agonists for 30 months was $13,620. Medical ADT requires good patient compliance to ensure frequent visits to a medical care facility which may not be optimal in resource-poor settings, giving surgical ADT yet another advantage [Table S1]. ADT is necessary only for a limited period of 24-36 months when it is used as neoadjuvant therapy. In such situations where reversibility is important, medical ADT is more advantageous [Table S1].

The choice of ADT should be individualized depending on the patient's clinical indication, life expectancy, compliance and patient's wishes. The cost of treatment should not be forgotten, more so, in resource-poor settings like Sri Lanka [11]. When counselling patients to decide on the type of ADT, it is important to consider the non-inferiority of surgical androgen ablation to medical forms of ADT. Accurate

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Received: 29-05-2022 Accepted: 24-06-2022
DOI: http://doi.org/10.4038/sljs.v40i2.8967

evidence should be provided to the patients so that they could make informed decisions regarding their management.

All authors disclose no conflict of interest. The study was conducted in accordance with the ethical standards of the relevant institutional or national ethics committee and the Helsinki Declaration of 1975, as revised in 2000.

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