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Original article

Decision analysis defining optimal management of clinical stage 1 high-risk nonseminomatous germ cell testicular cancer with lymphovascular invasion

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Abstract

Background: Risk of recurrent disease for men with clinical stage 1 high-risk nonseminomatous germ cell testicular cancer (CS1 NSGCT) with lymphovascular invasion (LVI) after orchiectomy is 50% and current treatment options (surveillance [S], retroperitoneal lymph node dissection [RPLND], or 1 cycle of BEP [BEP ×1]) are associated with a 99% disease specific survival, therefore practice patterns vary. We performed a decision analysis using updated data of long-term complications for men with CS1 NSGCT with LVI to quantify and assess relative treatment values.

Methods: Decision analysis included previously defined utilities (via standard gamble) for posttreatment states of living from 0 (death from disease) to 1 (alive in perfect health) and updated *morbidity* probabilities. We quantified the values of S, RPLND, and BEP ×1 via the rollback method. Sensitivity analyses including a range of orchiectomy cure rates and utility values were performed.

Results: Estimated probabilities favoring treatment with RPLND (0.97) or BEP ×1 (0.97) were equivalent and superior to surveillance (0.88). Sensitivity analysis of orchiectomy cure rates (50%–100%) failed to find a cure rate that favored S over BEP ×1 or RPLND. Varying utility values for cure after S from 0.92 (previously defined utility) to 1 (perfect health), failed to find a viable utility state favoring S over BEP ×1 or RPLND. An orchiectomy cure rate of ≥82% would be required for S to equal treatment of either type.

Conclusions: We demonstrate that for surveillance to be superior to treatment with BEP ×1 or RPLND, the orchiectomy cure rate must be at least 82%, which is not expected in a patient population with high-risk CS1 NSGCT.

Keywords: High-risk CS1 NSGCTs; Decision analysis; Patient utilities; Treatment algorithm; Treatment value

1. Introduction

Primary treatment of clinical stage I nonseminomatous germ cell tumor (CS1 NSGCT) is guided by expert opinion and varies by institution [1–5]. Acceptable treatment options include surveillance (S), retroperitoneal lymph node dissection (RPLND), or 1 cycle of chemotherapy with bleomycin, etoposide and cisplatin (BEP ×1) [6]. Risk-adapted approach further classifies CS1 NSGCT into high risk if there is evidence of lymphovascular invasion (LVI) or the embryonal carcinoma component is >50%. However, although risk of recurrence under surveillance for high-risk CS1 NSGCT increases from 30% to 50%, disease specific survival after adjuvant or salvage treatment reaches 99% and therefore treatment selection remains variable [7–9].

Current controversy is whether to treat or observe high-risk CS1 NSGCT. Previous study by Nguyen et al. [10] investigated the merit of a decision analysis to mathematically distinguish the value of each treatment for CS1 NSGCT taking into account oncological outcomes, treatment-related toxicities and patient preferences. They found that treatment is preferred over surveillance only when the risk of relapse

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after orchiectomy is 46%–54%, that is, for high-risk CS1 NSGCT. We performed a decision analysis in men with high-risk CS1 NSGCT as defined by the presence of LVI while using updated morbidity data including long-term complications to compare treatment values.

2. Methods

2.1. Decision tree modeling

Decision tree model was used to calculate and compare the values of each treatment (S, RPLND, or BEP ×1) in CS1 NSGCT with LVI. We incorporated probabilities of survival, recurrence, and treatment-related outcomes obtained from updated literature, including recently published data regarding recurrence risks and long-term treatment-related morbidity [11–20]. Model's purpose was to investigate long-term outcomes, therefore morbidities that occurred during treatment period and subsequently resolved were excluded. Most patients who receive chemotherapy for relapsed disease only require first line of therapy [7,9]. Treatment regimens used for second line therapy and beyond are infrequently necessary and heterogeneous, limiting the ability to precisely quantify the morbidities. As such, we grouped all morbidity probabilities among patients who received chemotherapy beyond BEP ×1 into 1 group.

Decision tree presented in Fig. 1 summarizes potential treatment course and outcomes for a patient with CS1 NSGCT with LVI who is status post orchiectomy; this is the time of treatment decision in the model. For patients managed with S (Fig. 1B), there is a 50% chance of cure with orchiectomy alone [7,9,21,22]. Remaining 50% of patients who relapse are treated with induction chemotherapy [7,9,22]. Of those treated with chemotherapy, 69% are cured with chemotherapy alone, 26% have persistent disease and undergo RPLND, and 5% relapse after initial complete response to induction chemotherapy [7]. Among those that undergo surgery for persistent disease, approximately 87% are cured; remaining 13% receive salvage chemotherapy, of which approximately 50% are cured and 50% die from disease [7,10,23]. Among those that relapse following induction chemotherapy and receive salvage chemotherapy or surgery, approximately 50% are cured and 50% die of disease [10].

For patients treated with RPLND (Fig. 1C), there is a 68% chance of cure with RPLND alone [24]. Remaining patients are either upstaged to pathologic stage II disease and require adjuvant chemotherapy (approximately 20%) [24,25], or relapse (remaining 12%) [24]. Of those who are upstaged and receive adjuvant chemotherapy, 94% are cured and 6% relapse and require additional chemotherapy, which results in cure in approximately 50% and death with disease in 50% [10,25,26]. Of those who relapse after RPLND alone and receive salvage chemotherapy, 95% are

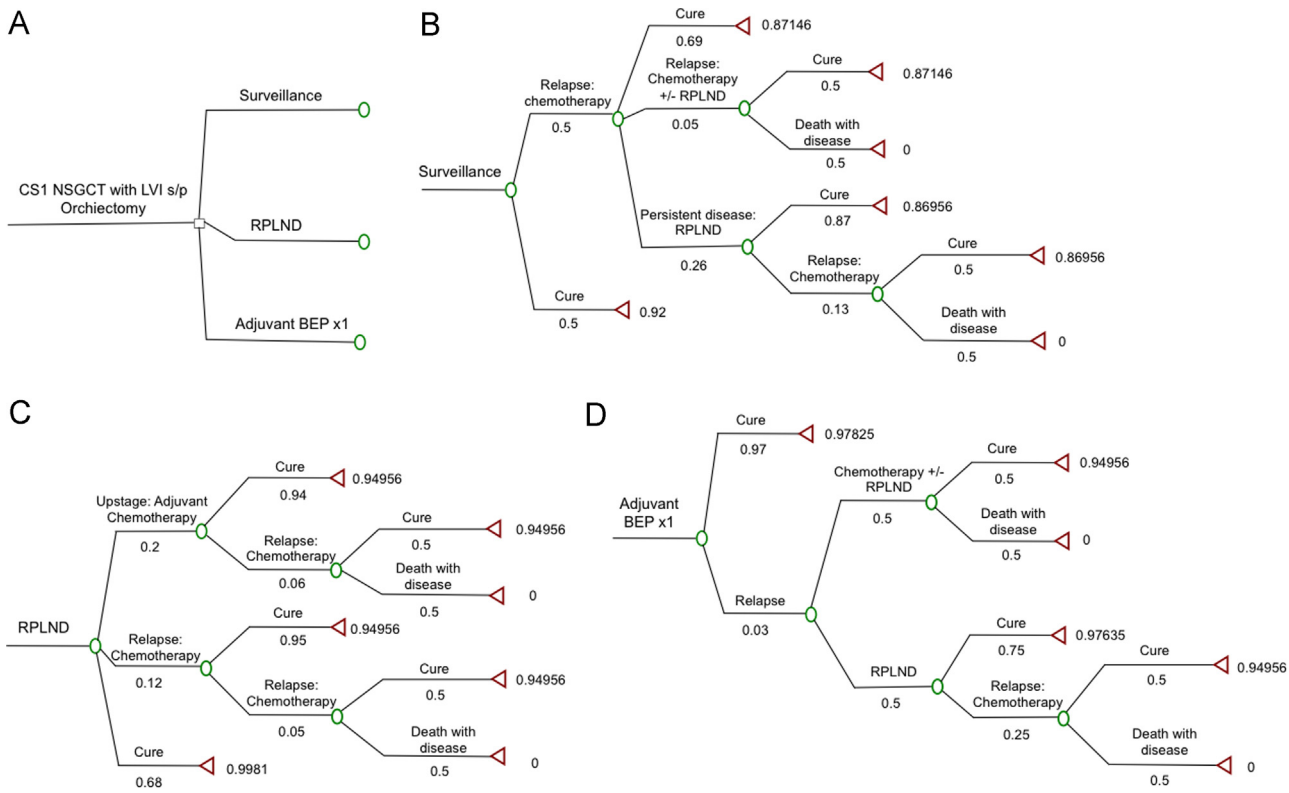

Fig. 1. Standard gamble decision tree. (A) Time of treatment decision for a patient with CS1 NSGCT following orchiectomy. (B) Surveillance. (C) RPLND. (D) BEP ×1. (Color version of the figure available online.)