Adoption of concurrent chemoradiation in stage 2 nasopharyngeal cancer (NPC) and its effect on mortality in the era of intensity modulated radiation therapy techniques: A population-based outcomes study

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Background

A landmark Chinese randomized phase 3 trial published in 2011 demonstrated a significant improvement in overall survival (hazard ratio (HR) of 0.3) in patients with stage 2 NPC with the use of upfront concurrent chemotherapy (CC) and two-dimensional (2D) radiation therapy (RT) compared to 2D RT alone. However, it is unclear if this landmark trial can affect routine clinical practice and whether the large magnitude of benefit observed in the trial can be reproduced at population level in the era of intensity modulated radiation therapy (IMRT) techniques. This study aims to determine the impact of this landmark trial on the adoption of upfront CCRT in stage 2 NPC and whether the survival benefit of CC seen in the trial can be reproduced in the real-world setting.

Methods

All patients diagnosed with stage 2 NPC in Singapore from 2003 - 2017 were identified using the Singapore Cancer Registry. We described and compared the trends in adoption of upfront CCRT for those diagnosed in 2003 - 2011 to those diagnosed in 2012 - 2017. We also compared the 5-year relative survival trends for patients diagnosed from 2003 to 2011 to those diagnosed from 2012 to 2013. The significance of changes in trends of adoption rate of CCRT and 5-year survival rates were examined using interrupted time series (ITS) analysis. Multivariable Cox regression was used to analyze the overall survival differences between those receiving CCRT and RT.

Findings

There were 778 patients with stage 2 NPC. Their median age was 51 years old. Majority were male (73%) and Chinese (95%). While the adoption rate of CC increased from 7% in 2003 to 42% in 2017, there was no significant difference in the rate of increase between the time periods of 2003-2011 and 2012-2017. The 5-year relative survival fluctuated over the years, with no significant difference in the 5-year relative survival trends between the time periods of 2003-2011 and 2012-2013. There was no significant difference in overall survival between CCRT and RT when adjusted for age, gender, race and nodal status in 2003-2011 (HR: 0.66, 95% CI 0.38 - 1.14) and 2012-2017 (HR: 1.10, 95% CI 0.25 - 4.79).

Conclusions

The publication of the landmark trial in 2011 **did not have an impact** on the adoption of upfront CCRT for stage 2 NPC. **The survival benefit of CC in the landmark trial could not be reproduced in the real-world settings** in the era of routine IMRT techniques.

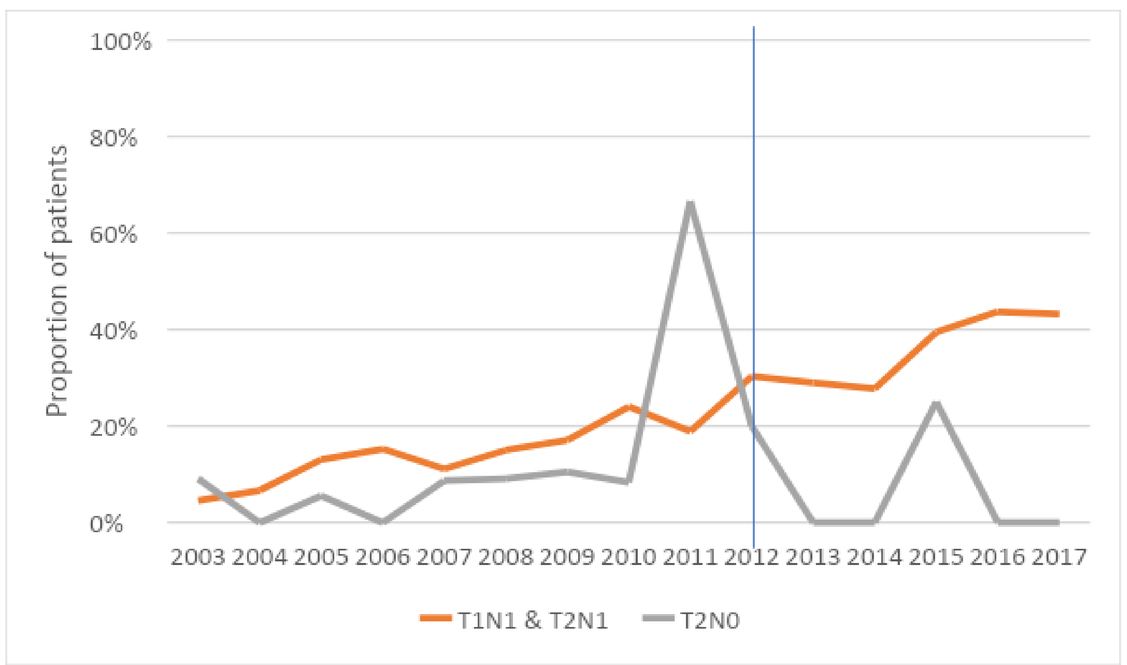

Figure 1. Adoption of CCRT in stage 2 NPC diagnosed from 2003 to 2017

	T1 N1, T2N1 Coefficient (95% CI)	T2 N0 Coefficient (95% CI)
Difference in trend of adoption of CCRT between stage 2 and stage 1 in pre-adoption period	0.59% (0.22% to 0.96%)	1.17% (0.15% to 2.18%)
Difference in change of adoption of CCRT between stage 2 and stage 1 in first three months of post-adoption period	2.51% (-11.36% to 16.39%)	-11.02% (-43.76% to 21.72%)
Difference in trend of adoption of CCRT between stage 2 and stage 1 in post- adoption period minus Difference in trend of adoption of CCRT between stage 2 and stage 1 in pre-adoption period	0.11% (-0.79% to 1.01%)	-1.99% (-4.04% to 0.05%)
Difference in trend of adoption of CCRT between stage 2 and stage 1 in post-adoption period	0.70% (-0.11% to 1.51%)	-0.83% (-2.48% to 0.83%)

Table 1. Comparison of adoption of CCRT among patients diagnosed with stage 2 NPC in the pre- and post-adoption periods

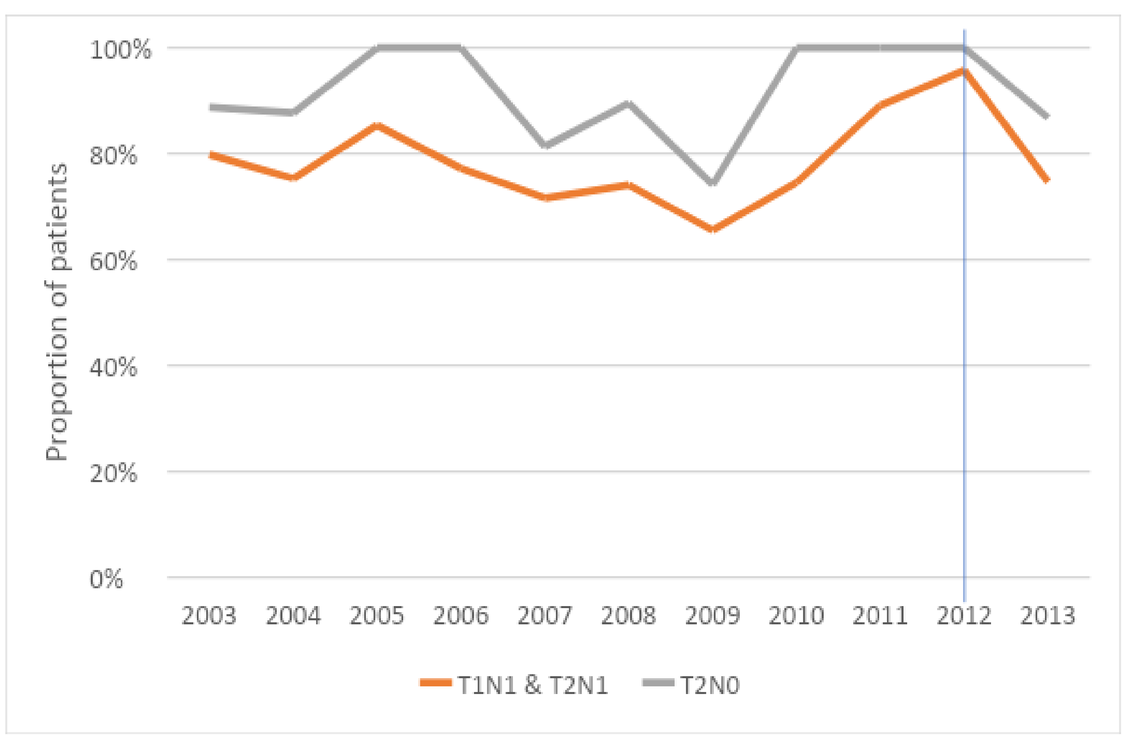

Figure 2. 5-year relative survival of stage 2 NPC diagnosed from 2003 to 2013

	T1 N1, T2N1 Coefficient (95% CI)
Trend of 5-year relative survival in pre-adoption period	-0.27% (-0.68% to 0.14%)
Difference in 5-year relative survival in first three months of post-adoption period	6.02% (-10.88 % to 22.92%)
Difference in trend of 5-year relative survival between pre- and post-adoption periods	1.27% (-2.12% to 4.67%)
Trend of 5-year relative survival in post-adoption period	1.00% (-2.34% to 4.34%)

*Comparison of 5-year relative survival among stage 2 N0 NPC patients in the pre- and post-adoption periods could not be done due to insufficient number of events

Table 2. Comparison of 5-year relative survival among stage 2 N1* NPC patients in the pre- and post-adoption periods