Introduction

Numerous clinical trials have demonstrated survival improvements with the addition of chemotherapy to definitive radiation therapy (RT) for head and neck cancers, as highlighted by the MACH-NC meta-analysis [1]. One important result of this study, however, was a decreasing benefit to chemotherapy with increasing age, which was independent of other covariates analyzed. Moreover, nearly 40% of deaths in patients ≥71 years of age therein were not cancer-related. Although the meta-analysis did not evaluate toxicities, numerous studies have illustrated decreased tolerance of oncologic therapies by older patients [2–4].

A factor limiting applicability of the MACH-NC report was its specific exclusion of nasopharyngeal cancer (NPC). This neoplasm, rare in the United States but endemic in south China and north Africa, is most commonly treated with chemoradiotherapy (CRT) [5]. This paradigm is supported by the MAC-NPC meta-analysis, which...
Materials & Methods

The NCDB is a joint project of the Commission on Cancer (CoC) of the American College of Surgeons and the American Cancer Society, which consists of de-identified information regarding tumor characteristics, patient demographics, and patient survival for approximately 70% of the United States population [8–15]. All pertinent cases are reported regularly from CoC-accredited centers and compiled into a unified dataset, which is then validated. The NCDB contains information not included in the Surveillance, Epidemiology, and End Results database, including details regarding use of systemic therapy. The data used in the study were derived from a de-identified NCDB file (2004–2013). The American College of Surgeons and the CoC have not verified and are neither responsible for the analytic or statistical methodology employed nor the conclusions drawn from these data by the investigators. As all patient information in the NCDB database is de-identified, this study was exempt from institutional review board evaluation.

Inclusion criteria for this study were patients ≥70 years of age with newly-diagnosed nasopharyngeal cancer treated with RT for curative intent. The 70-year-old threshold was utilized because it is among the most commonly used cutoff to denote “older” patients in head/neck cancer as well as many other areas of oncology [16]; it is also close to the threshold utilized in the MACH-NC study [1]. T1N0 and M1 cases were excluded because CRT is not the consensus-based recognized treatment for these subsets; patients receiving any form of pharyngectomy were similarly removed because it is nonstandard for NPC and to isolate the effect of adding chemotherapy to RT [5]. Other exclusion criteria were incomplete chemotherapy to RT [6]. Just 13% of the total MAC-NPC cohort was ≥60 years of age; although the proportion ≥70 years old was not reported, it is likely less than half of that figure.

As a result, optimal management for older (defined as ≥70 years old herein) NPC patients with respect to the additional chemotherapy is currently not well defined. Although challenging to assess with single- or multi-institutional analyses owing to the relative rarity of older NPC patients, the National Cancer Data Base (NCDB) provides a unique resource with which to address this novel but clinically important issue. In this investigation, the largest such study to date, we evaluated national practice patterns and outcomes in older NPC patients treated with CRT versus RT alone.

Results

A complete flow diagram of patient selection is provided in Figure 1. In total, 930 patients met study analysis criteria. Table 1 displays notable clinical characteristics of the analyzed patients, most (74%) of whom were 70–79 years of age. A total of 713 (77%) patients underwent CRT, whereas 217 (23%) received RT alone. After univariable analysis was performed to assess factors associated with receipt of CRT, multivariable assessment revealed that factors independently associated with decreased likelihood of CRT delivery were advancing age (P = 0.001), female gender (P = 0.014), and node-negative disease (P = 0.002). There was also a trend toward increasing CRT receipt in more recent years (2009–2013, P = 0.063).

Median follow-up was 23 months (range, 0–129 months). Kaplan–Meier estimates comparing OS in patients that received RT alone versus CRT are illustrated in Figure 2; median OS in the respective cohorts were 20.0 (95% confidence interval (CI), 12.8–27.3) months and 35.3 (95% CI, 29.3–41.2) months (P = 0.002).

In the overall cohort, there were several predictors of OS on univariate analysis (Table 2). After multivariate adjustment for potential confounding factors (Table 2), factors independently associated with poorer OS included advancing age, comorbidity index, lower income, Medicare insurance (relative to private), poor/undifferentiated/anaplastic disease, and stage IV (M0) disease (P < 0.05 for all). Of note, receipt of CRT relative to RT alone independently predicted for improved OS (hazard ratio, 0.721, 95% CI, 0.532–0.979, P = 0.036).
Discussion

To the best of our knowledge, this is the largest report assessing practice patterns and outcomes of RT with or without chemotherapy for elderly NPC patients. Our study of a large national database of this relatively uncommon clinical circumstance notably demonstrates that the addition of chemotherapy to RT is independently associated with greater survival in older patients, indicating that the benefit of chemotherapy in NPC may extend potentially to all ages.

A main message from our analysis is that causation is not implied; it could very well be that patients receiving RT alone were not healthy enough to receive additional chemotherapy, and hence they would naturally do worse and be at greater risk of dying from noncancer causes as mentioned above. Although the lack of endpoints such as cancer-specific survival and local/regional control in the NCDB hampers firm conclusions, there are several reasons to believe this bias may be relatively minimal. First, cohorts were relatively balanced, including no differences in Charlson-Deyo comorbidity index (although this does not equate to performance status, it did independently predict for OS on Cox multivariate analysis herein). In fact, because groups were overall quite balanced,
Table 1. Characteristics of the overall cohort and factors associated with receiving chemoradiotherapy.

| Parameter, N (%) or median (range) | CRT (N = 713) | RT Alone (N = 217) | Univariable | Multivariable (stepwise) |
|-----------------------------------|---------------|-------------------|-------------|--------------------------|
|                                   |               |                   | OR (95% CI) | P-value                  |
|                                   |               |                   | OR (95% CI) | P-value                  |
| Age (years)                       |               |                   |             |                          |
| Median (range)                    | 75 (70–90)    | 79 (70–90)        | 0.542 (0.398–0.737) | 0.001                  |
| Gender                            |               |                   |             |                          |
| Male                              | 467 (66%)     | 110 (51%)         | 1.161 (1.125–1.198) | 0.001                  |
| Female                            | 246 (34%)     | 107 (49%)         | REF         |                          |
| Race                              |               |                   |             |                          |
| White                             | 522 (73%)     | 166 (76%)         | REF         |                          |
| Black                             | 65 (9%)       | 18 (8%)           | 0.871 (0.502–1.510) | 0.622                  |
| Other                             | 106 (15%)     | 26 (12%)          | 0.771 (0.485–1.226) | 0.272                  |
| Unknown                           | 20 (3%)       | 7 (3%)            | REF         |                          |
| Charlson deyo score¹              |               |                   |             |                          |
| 0                                 | 541 (76%)     | 158 (73%)         | REF         |                          |
| 1                                 | 129 (18%)     | 43 (20%)          | 1.141 (0.774–1.682) | 0.504                  |
| ≥2                                | 43 (6%)       | 16 (7%)           | 1.274 (0.699–2.323) | 0.429                  |
| Insurance type                    |               |                   |             |                          |
| Uninsured                         | 3 (0%)        | 0 (0%)            | –           | –                       |
| Private                           | 88 (12%)      | 29 (13%)          | 1.098 (0.699–1.727) | 0.684                  |
| Medicaid/Other Government (non-Medicare) | 31 (4%)   | 10 (5%)           | 1.075 (0.517–2.237) | 0.846                  |
| Medicare                          | 580 (81%)     | 174 (80%)         | REF         |                          |
| Unknown                           | 9 (1%)        | 4 (2%)            | –           | –                       |
| Income (US dollars/year)          |               |                   |             |                          |
| <$30,000                          | 127 (18%)     | 44 (20%)          | REF         |                          |
| $30,000–$34,999                   | 157 (22%)     | 52 (24%)          | 0.956 (0.601–1.521) | 0.849                  |
| $35,000–$45,999                   | 195 (27%)     | 57 (26%)          | 0.844 (0.537–1.326) | 0.462                  |
| ≥$46,000                          | 226 (32%)     | 57 (26%)          | 0.728 (0.464–1.141) | 0.166                  |
| Unknown                           | 6 (1%)        | 7 (3%)            | –           | –                       |
| Location                          |               |                   |             |                          |
| Metro                             | 596 (84%)     | 174 (80%)         | REF         |                          |
| Urban                             | 85 (12%)      | 31 (14%)          | 1.249 (0.801–1.949) | 0.327                  |
| Rural                             | 9 (1%)        | 2 (1%)            | 0.761 (0.163–3.556) | 0.761                  |
| Unknown                           | 23 (3%)       | 10 (5%)           | –           | –                       |
| Percentage of adults in zip code without high school diploma |           |                   |             |                          |
| ≥21%                              | 137 (19%)     | 38 (18%)          | REF         |                          |
| 13–20.9%                          | 186 (26%)     | 61 (28%)          | 1.182 (0.745–1.875) | 0.477                  |
| 7–12.9%                           | 233 (33%)     | 68 (31%)          | 1.052 (0.671–1.649) | 0.825                  |
| <7%                               | 149 (21%)     | 44 (20%)          | 1.065 (0.651–1.742) | 0.803                  |
| Unknown                           | 8 (1%)        | 6 (3%)            | –           | –                       |
| Facility type                     |               |                   |             |                          |
| Community                         | 385 (54%)     | 134 (62%)         | REF         |                          |
| Academic                          | 328 (46%)     | 83 (38%)          | 1.375 (1.008–1.877) | 0.044                  |
| Facility location                 |               |                   |             |                          |
| Northeast                         | 174 (24%)     | 39 (18%)          | REF         |                          |
| South                             | 223 (31%)     | 76 (35%)          | 0.752 (0.461–1.227) | 0.254                  |
| Midwest                           | 175 (25%)     | 60 (28%)          | 1.144 (0.743–1.762) | 0.541                  |
| West                              | 141 (20%)     | 42 (19%)          | 1.151 (0.732–1.810) | 0.542                  |
| Distance to treating facility (mi) |           |                   |             |                          |
| Median (range)                    | 8 (0–2456)    | 7 (0–1736)        | 1.000 (0.999–1.001) | 0.510                  |
| Year of Diagnosis                 |               |                   |             |                          |
| 2004–2008                         | 330 (46%)     | 117 (54%)         | 0.736 (0.543–0.999) | 0.049                  |
| 2009–2013                         | 383 (54%)     | 100 (46%)         | REF         | 0.723 (0.514–1.017) | 0.063                  |
| Tumor grade                       |               |                   |             |                          |
| Well or moderate                   | 138 (19%)     | 38 (18%)          | REF         |                          |
| Poorly, undifferentiated, anaplastic | 384 (54%) | 99 (46%)          | 1.068 (0.701–1.628) | 0.759                  |
| Unknown                           | 191 (27%)     | 80 (37%)          | –           | –                       |

(Continued)
there was relatively little indication for propensity matching, which would have prohibitively eliminated sample size from an already limited patient population. Furthermore, there were only three variables significantly different between groups on multivariable logistic regression analysis (age, gender, and nodal status); of those three variables, the CRT cohort was younger but had a higher proportion of node-positive disease and males. Younger age has been shown to associate with more advanced disease [17]; node-positivity and male gender also correlate with poorer prognosis [18–20]. In this manner, consistent with other work, it is plausible that chemotherapy potentially may have been given to a “higher-risk” population, and that there may be “true” benefits to adding chemotherapy [21, 22].

Despite the large dataset offered by the NCDB, one of its major limitations is a lack of toxicity assessment. To this extent, smaller retrospective reports of older NPC patients (which have employed varying definitions of “older/elderly”) suggest that despite the increase in acute toxicities when adding chemotherapy to RT, these may not be worse in severity from those experienced by younger patients [23, 24]. This is consistent with multiple studies in other head/neck neoplasms showing similar toxicities and/or outcomes in elderly patients as compared to their younger counterparts [2, 25–27]. Thus, we encourage judicious and individualized judgment when evaluating administration of CRT in elderly NPC patients; there will likely never be a “definitive answer” regarding aggressive therapies (vs. lack thereof) in elderly patients, owing to retrospective patient selection biases and varying definitions of “older/elderly” patients from study to study.

We, therefore, propose that the term “older/elderly” should not be singularly defined by age, because these patients are intrinsically heterogeneous [28]. Rather, utilization of many available measures to measure functionality (e.g., the Comprehensive Geriatric Assessment) and

| Parameter, N (%) or median (range) | CRT (N = 713) | RT Alone (N = 217) | Univariable OR (95% CI) | Multivariable (stepwise) OR (95% CI) |
|-----------------------------------|--------------|--------------------|------------------------|--------------------------------------|
| T classification                  |              |                    |                        |                                      |
| X                                 | 21 (3%)      | 6 (3%)             | REF                    |                                      |
| 1                                 | 147 (21%)    | 33 (15%)           | 1.577 (0.282–8.808)    | 0.604                                |
| 2                                 | 203 (28%)    | 72 (33%)           | 0.708 (0.443–1.132)    | 0.149                                |
| 3                                 | 137 (19%)    | 41 (19%)           | 1.119 (0.759–1.648)    | 0.571                                |
| 4                                 | 205 (29%)    | 65 (30%)           | 0.944 (0.604–1.475)    | 0.800                                |
| N classification                  |              |                    |                        |                                      |
| 0                                 | 193 (27%)    | 103 (47%)          | 0.396 (0.238–0.554)    | 0.001                                |
| 1                                 | 237 (33%)    | 53 (24%)           | 0.630 (0.127–1.133)    | 0.238                                |
| 2                                 | 196 (27%)    | 43 (20%)           | 0.661 (0.161–1.161)    | 0.263                                |
| 3                                 | 52 (7%)      | 7 (3%)             | REF                    |                                      |
| Unknown                           | 35 (5%)      | 11 (5%)            | REF                    |                                      |
| Group stage                       |              |                    |                        |                                      |
| I                                 | 94 (13%)     | 34 (16%)           | 1.370 (0.858–2.186)    | 0.187                                |
| II                                | 233 (33%)    | 64 (29%)           | 1.040 (0.714–1.515)    | 0.837                                |
| III                               | 284 (40%)    | 75 (35%)           | REF                    |                                      |
| IV                                | 102 (14%)    | 44 (20%)           | REF                    |                                      |

Statistically significant P-values (P < 0.05) are in bold. Only values included in the final multivariable model are shown. CRT, chemoradiotherapy; RT, radiotherapy; OR, odds ratio; CI, confidence interval.

The Charlson-Deyo index is a weighted score of comorbidities as defined by several medical codes.
performance status (PS) is a more reliable way to divide “older/elderly” patients into the “functionally older/elderly” or “functionally young” [29]. For instance, Liu and colleagues did not find a benefit to adding chemotherapy to RT in NPC patients with high comorbidity indices [23]. This study was underpowered to confirm those findings. Nevertheless, these and other parameters are critically important in adequately selecting “elderly” patients that are “fit” to receive aggressive oncologic therapies.

Lastly, although one method to reduce toxicities of CRT is delivering chemotherapy and RT sequentially, we were unable to separately ascertain the benefit of concurrent versus sequential CRT. In our dataset, a large majority (77%) of CRT patients received chemotherapy and RT within 2 weeks of each other (two weeks being a previously utilized cutoff point for concurrent therapy in prior such publications [30]). Of the remaining 23% of the CRT cohort, timing of therapies was unknown in 7%, indicating that just 16% certainly received sequential CRT. This was much too small of a sample size to analyze separately in this study. Hence, induction chemotherapy followed by RT remains an attractive option in well-selected “older” NPC patients at higher risk of toxicities. Additionally, although the use of induction chemotherapy

### Table 2. Univariate and multivariate Cox proportional hazards model for overall survival.

| Parameter                                      | Univariate HR | 95% CI      | P-value | Multivariate HR | 95% CI      | P-value |
|------------------------------------------------|---------------|-------------|---------|----------------|-------------|---------|
| Treatment group (CRT vs. RT alone)             | 0.735         | 0.606–0.892 | 0.002   | 0.721          | 0.532–0.979 | 0.036   |
| Age (continuous)                               | 1.053         | 1.036–1.069 | 0.001   | 1.063          | 1.037–1.090 | 0.001   |
| Gender (male vs. female)                       | 0.864         | 0.725–1.030 | 0.163   |                |             |         |
| Race (black vs. white)                         | 0.845         | 0.625–1.144 | 0.276   |                |             |         |
| Race (other vs. white)                         | 0.262         | 0.468–0.823 | 0.001   |                |             |         |
| Charlson–Deyo score (0 vs. 2)                  | 0.517         | 0.377–0.710 | 0.001   | 0.517          | 0.377–0.710 | 0.001   |
| Charlson–Deyo score (1 vs. 2)                  | 0.609         | 0.426–0.872 | 0.007   | 0.609          | 0.426–0.872 | 0.001   |
| Insurance (uninsured vs. Medicare)             | 2.252         | 2.252–9.052 | 0.253   | 2.752          | 2.347–20.234| 0.320   |
| Insurance (private vs. Medicare)               | 0.613         | 0.459–0.852 | 0.001   | 0.553          | 0.359–0.852 | 0.007   |
| Insurance (Medicaid/other vs. Medicare)        | 0.629         | 0.387–1.022 | 0.061   | 0.700          | 0.377–1.298 | 0.257   |
| Income (<$30,000 vs. $30,000–$34,999)          | 1.584         | 1.233–2.035 | 0.001   | 1.584          | 1.233–2.035 | 0.001   |
| Income (<$30,000 vs. $35,000–$45,999)          | 1.403         | 1.097–1.794 | 0.019   | 1.403          | 1.097–1.703 | 0.007   |
| Income (<$30,000 vs. ≥$46,000)                 | 1.323         | 1.047–1.671 | 0.039   | 1.323          | 1.047–1.671 | 0.019   |
| Location (urban vs. metro)                     | 1.384         | 1.080–1.773 | 0.010   |                |             |         |
| Location (rural vs. metro)                     | 1.777         | 0.841–3.757 | 0.132   |                |             |         |
| Percentage of adults in zip code without high school diploma (13–20.9% vs. ≥21%) | 1.125         | 0.851–1.486 | 0.408   |                |             |         |
| Percentage of adults in zip code without high school diploma (7.9–12.9% vs. ≥21%) | 1.267         | 0.986–1.629 | 0.065   |                |             |         |
| Percentage of adults in zip code without high school diploma (<7% vs. ≥21%) | 1.049         | 0.820–1.341 | 0.704   |                |             |         |
| Facility type (academic vs. community)          | 1.146         | 0.962–1.366 | 0.126   |                |             |         |
| Facility location (South vs. Northeast)        | 1.143         | 0.867–1.507 | 0.344   |                |             |         |
| Facility location (Midwest vs. Northeast)      | 1.289         | 1.001–1.658 | 0.049   |                |             |         |
| Facility location (West vs. Northeast)         | 1.301         | 1.000–1.693 | 0.050   |                |             |         |
| Distance to treatment facility (continuous)    | 1.000         | 0.999–1.000 | 0.515   |                |             |         |
| Year of diagnosis (2004–2008 vs. 2009–2013)    | 0.981         | 0.815–1.182 | 0.843   |                |             |         |
| Grade (poor/undifferentiated/anaplastic vs. well/moderate) | 1.691         | 1.356–2.110 | 0.001   | 1.510          | 1.163–1.962 | 0.002   |
| T classification (x vs. 1)                     | 0.326         | 0.104–1.022 | 0.055   |                |             |         |
| T classification (x vs. 2)                     | 0.404         | 0.311–0.525 | 0.001   |                |             |         |
| T classification (x vs. 3)                     | 0.494         | 0.397–0.614 | 0.001   |                |             |         |
| T classification (x vs. 4)                     | 0.532         | 0.411–0.698 | 0.001   |                |             |         |
| N classification (0 vs. 1)                     | 0.548         | 0.379–0.792 | 0.001   |                |             |         |
| N classification (0 vs. 2)                     | 0.695         | 0.481–1.003 | 0.052   |                |             |         |
| N classification (0 vs. 3)                     | 0.612         | 0.426–0.879 | 0.008   |                |             |         |
| Group stage (II vs. IV)                        | 0.497         | 0.358–0.691 | 0.001   | 0.530          | 0.359–0.783 | 0.001   |
| Group stage (III vs. IV)                       | 0.619         | 0.505–0.759 | 0.001   | 0.550          | 0.423–0.716 | 0.001   |

Statistically significant P values (P < 0.05) are in bold. Only values included in the final multivariate model are shown.

HR, hazard ratio; CI, confidence interval; CRT, chemoradiotherapy; RT, radiotherapy.

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followed by CRT could emerge as a new standard of care [31], the phase III trial deliberately excluded patients ≥60 years of age owing to toxicity risks. However, retrospective data of patients ≥60 years treated with CRT with or without induction chemotherapy showed no outcome differences, with higher toxicities in those receiving induction therapy [32].

Although the NCDB provides a unique platform for studying this important clinical question, this investigation still has limitations. First, NCDB studies are inherently retrospective, with selection biases and lack of several endpoints as mentioned above. Second, NCDB does not keep track of precise chemotherapy details, including specific chemotherapeutic agents, reasons for withholding chemotherapy in RT alone patients (ie. related to tolerability vs. disease-related factors), or the number of cycles of chemotherapy received. Third, the NCDB does not allow for an assessment of subsequent lines of treatment (e.g., re-irradiation, further systemic and/or targeted therapy), which could influence OS. Furthermore, the NCDB also does not provide details such as performance/functional status, Epstein–Barr virus status, or radiotherapy field design/volumes/techniques. Fourth, a major limitation of this study was too few patients for a statistically reliable subset analysis of whether benefit to CRT is limited to patients with advanced versus limited nodal disease. The NCDB is also unique to the United States and thus may not be representative to other areas of the world where NPC is endemic.

Conclusions

This is the largest study to date evaluating the utility of CRT, as compared to RT alone, for older (≥70 years old) patients with NPC. Administration of CRT was independently associated with improved survival, but causation is not implied, and careful patient selection is necessary to balance treatment-related toxicity risks with potential oncologic benefits.

Conflict of Interest

None declared. This has never been presented/published before in any form. All authors declare that conflicts of interest do not exist.

References

1. Pignon, J. P., A. le Maitre, E. Maillard, W. J. Curran, K. Furuse, P. Fournel, et al. 2009. Meta-analysis of chemotherapy in head and neck cancer (MACH-NC): an update on 93 randomised trials and 17,346 patients. Radiother. Oncol. 92:4–14.

2. Verma, V., and A. K. Ganti. 2016. Concurrent chemoradiotherapy in older adults with squamous cell head & neck cancer: evidence and management. J. Geriatr. Oncol. 7:145–153.

3. Siddiqui, F., and C. K. Gwede. 2012. Head and neck cancer in the elderly population. Semin. Radiat. Oncol. 22:321–333.

4. VanderWalde, N. A., M. Fleming, J. Weiss, and B. S. Chera. 2013. Treatment of older patients with head and neck cancer: a review. Oncologist 18:568–578.

5. National Comprehensive Cancer Network. Head and neck cancers. Version 2.2017. Available at: https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf (last accessed: September 6, 2017).

6. Blanchard, P., A. Lee, S. Marguet, J. Leclercq, W. T. Ng, J. Ma, et al. 2015. Chemotherapy and radiotherapy in nasopharyngeal carcinoma: an update of the MAC-NPC meta-analysis. Lancet Oncol. 16:645–655.

7. American Cancer Society. What are the key statistics about nasopharyngeal cancer? Available at: https://www.cancer.org/cancer/nasopharyngeal-cancer/about/key-statistics.html (last accessed: September 6, 2017).

8. Bilimoria, K., A. Stewart, D. Winchester, C. Y. Ko. 2008. The national cancer data base: a powerful initiative to improve cancer care in the United States. Ann. Surg. Oncol. 15:683–690.

9. Stahl, J. M., C. D. Corso, V. Verma, H. S. Park, S. K. Nath, Z. A. Hussain, et al. 2017. Trends in stereotactic body radiation therapy for stage I small cell lung cancer. Lung Cancer 103:11–16.

10. Haque, W., V. Verma, E. B. Butler, and B. S. Teh. 2017. Patterns of care and outcomes of multi-agent versus single-agent chemotherapy as part of multimodal management of low grade glioma. J. Neurooncol. 133:369–375.

11. Haque, W., V. Verma, E. B. Butler, and B. S. Teh. 2017. National practice patterns and outcomes for T4b urothelial cancer of the bladder. Clin. Genitourin. Cancer. https://doi.org/10.1016/j.clgc.2017.08.013.

12. Moreno, A. C., V. Verma, W. L. Hofstetter, S. H. Lin. 2017. Patterns of care and treatment outcomes of elderly patients with stage I esophageal cancer: analysis of the National Cancer Data Base. J. Thorac. Oncol. 12:1152–1160.

13. McMillan, M. T., E. Ojerholm, V. Verma, K. A. Higgins, S. Singhal, J. D. Predina, et al. 2017. Radiation treatment time and overall survival in locally advanced non-small cell lung cancer. Int. J. Radiat. Oncol. Biol. Phys. 98:1142–1152.

14. Verma, V., J. M. Ryckman, C. B. Simone, II, and C. Lin. 2017. Patterns of care and outcomes with the addition of chemotherapy to radiation therapy for stage I nasopharyngeal cancer. Acta Oncol.. https://doi.org/10.1080/0284186X.2017.1351039.
15. Verma, V., C. A. Ahern, C. G. Berlind, W. D. Lindsay, S. Sharma, J. Shabason, et al. 2017. National cancer data base report on pneumonectomy versus lung-sparing surgery for malignant pleural mesothelioma. J. Thorac. Oncol. https://doi.org/10.1016/j.jtho.2017.08.012.

16. Gugic, J., and P. Strojan. 2013. Squamous cell carcinoma of the head and neck in the elderly. Rep. Pract. Oncol. Radiother. 18:16–25.

17. Wu, S. G., X. L. Liao, Z. Y. He, L. Y. Tang, X. T. Chen, Y. Wang, et al. 2017. National cancer data base report on pneumonectomy versus lung-sparing surgery for malignant pleural mesothelioma. J. Thorac. Oncol.. https://doi.org/10.1016/j.jtho.2017.08.012.

18. Gugic, J., and P. Strojan. 2013. Squamous cell carcinoma of the head and neck in the elderly. Rep. Pract. Oncol. Radiother. 18:16–25.

19. Wu, S. G., X. L. Liao, Z. Y. He, L. Y. Tang, X. T. Chen, Y. Wang, et al. 2017. National cancer data base report on pneumonectomy versus lung-sparing surgery for malignant pleural mesothelioma. J. Thorac. Oncol.. https://doi.org/10.1016/j.jtho.2017.08.012.

20. Verma, V., M. T. McMillan, S. Grover, and C. B. Simone. 2017. Stereotactic body radiation therapy and the influence of chemotherapy on overall survival for large (≥5 centimeter) non-small cell lung cancer. Int. J. Radiat. Oncol. Biol. Phys. 97:146–154.

21. Liu, H., Q. Y. Chen, L. Guo, L. Q. Tang, H. Y. Mo, Z. L. Zhong, et al. 2013. Feasibility and efficacy of chemoradiotherapy for elderly patients with a locoregionally advanced nasopharyngeal carcinoma: results from a matched cohort analysis. Radiat. Oncol. 8:70.

22. Zeng, Q., Y. Q. Xiang, P. H. Wu, X. Lv, C. N. Qian, and X. Guo. 2015. A matched cohort study of standard chemo-radiotherapy versus radiotherapy alone in elderly nasopharyngeal carcinoma patients. PLoS ONE 10:e0119593.

23. Zeng, Q., Y. Q. Xiang, P. H. Wu, X. Lv, C. N. Qian, and X. Guo. 2015. A matched cohort study of standard chemo-radiotherapy versus radiotherapy alone in elderly nasopharyngeal carcinoma patients. PLoS ONE 10:e0119593.

24. Verma, V., J. M. Rwigema, S. Adeberg, and C. B. Simone II. 2017. Enrollment of elderly patients with locally advanced non-small cell lung cancer in multi-institutional trials of proton beam radiation therapy. Clin. Lung Cancer 18:441–443.

25. Peters, T. T., B. F. van der Laan, B. E. Plaat, J. Wedman, J. A. Langendijk, and G. B. Halmos. 2011. The impact of comorbidity on treatment-related side effects in older patients with laryngeal cancer. 47:56–61.

26. Moye, V. A., S. Chandramouleswaran, N. Zhao, H. B. Muss, M. C. Weissler, D. N. Hayes, et al. 2015. Elderly patients with squamous cell carcinoma of the head and neck and the benefit of multimodality therapy. Oncologist 20:159–165.