Re: Subcentimeter Pulmonary Nodules Are Not Associated with Disease Progression in Patients with Renal Cell Carcinoma
Mano R, Vertosick E, Sankin AI, et al
J Urol 2015;193:776–82

Expert’s summary:
The authors assessed the prognostic value of the presence of indeterminate pulmonary nodules (IPNs) in patients receiving surgery for nonmetastatic renal cell carcinoma (RCC) by comparing the development of lung or any distant metastasis and death from RCC between patients with and without chest computed tomography (CT) within 6 mo before surgery.

Patients with less favorable clinical tumor characteristics were selected to undergo preoperative chest CT. Overall, the CT cohort had worse outcomes; however, in patients with American Joint Committee on Cancer (AJCC) stage I, no difference in outcomes was seen between patients receiving or not receiving chest CT.

Overall, 51% of patients with chest CT had IPNs. The 5-yr Kaplan-Meier estimation showed that 27% of patients with IPNs between 1 and 2 cm developed lung metastases compared with 10% of those with subcentimeter nodes and 9% of those without IPNs. IPNs sized 1–2 cm but not the presence of IPNs was a risk factor for any outcome in multivariable analysis. Addition of IPN size to a model based on stage, size, and histology slightly increased the discriminative ability for lung or any distant metastasis but not for RCC death.

Expert’s comments:
Although limited by its retrospective value, the study by Mano et al is interesting. Their data support the irrelevance of subcentimeter IPNs in the preoperative setting.

Major guidelines currently recommend thorax imaging at staging, but there is a lack of unanimity about the test [1,2]. The European Association of Urology recommends CT, whereas the National Comprehensive Cancer Network does not specify a type of imaging.

The implications of the presented study are clear. With respect to chest staging, a risk-adapted approach should be considered. With respect to follow-up, a proactive policy in patients with 1- to 2-cm IPNs is justified for those that support metastasectomy [3]. Meanwhile, a nihilistic approach will be undertaken by those that consider the absence of curative treatment or systemic therapy delay for metastatic RCC [4].

To change clinical practice based on retrospective studies seems premature and risky, but these meaningful results set the foundation for an international prospective assessment at a time when around 68% of tumors are cT1.

Conflicts of interest: The author has nothing to disclose.

References

M. Pilar Laguna
Department of Urology, AMC, University of Amsterdam, Amsterdam, The Netherlands
E-mail address: m.p.lagunas@amc.uva.nl.

http://dx.doi.org/10.1016/j.eururo.2015.07.066

Re: Clinical Efficacy of Collagenase Clostridium histolyticum in the Treatment of Peyronie’s Disease by Subgroups: Results from Two Large, Double-blind, Randomized, Placebo-controlled, Phase III Studies
Lipshultz LI, Goldstein I, Seftel AD, et al
BJU Int 2015;116:650–6

Experts’ summary:
The clinical efficacy of intralesional collagenase Clostridium histolyticum (CCH) as a treatment for Peyronie’s disease (PD) has been studied in two double-blind, randomized, placebo-controlled, multicenter studies (Investigation for Maximal Peyronie’s Reduction Efficacy and Safety Studies [IMPRESS] I and II) that included large patient populations (418 patients each; 2:1 treatment:placebo ratio). This subsequent study assessed the curvature degree and PD symptom-bother reduction efficacy for subgroups derived from the two previous studies. The subgroups were stratified by penile curvature deformity (30–60°, 60–90°), PD onset duration (1–2, 2–4, >4 yr), penile calcification level (no calcification, noncontiguous stippling, and contiguous calcification), and erectile function (EF; International Index of Erectile Function–Erectile Function domain [IIEF-EF] scores: 1–5, 6–16, ≥17; no sexual activity, low and high EF, respectively). Adult sexually active patients (aged >18 yr) with PD >1 yr were administered CCH treatment, as defined in the previous IMPRESS studies.

CCH therapy was superior to placebo in terms of curvature and PD symptom-bother reduction in all subgroups. The reduction in degree of curvature was significantly superior for CCH in both the 30–60° and 60–90° groups, but difference in reduction of symptom bother did
not reach significance in the 60–90° group (p = 0.071). In the PD duration stratification, although CCH was not significantly superior to placebo in the group with onset duration of 1–2 yr, it proved superior for curvature reduction in the group with onset duration of 2–4 yr and for both aspects of the group with onset duration of >4 yr. CCH treatment was statistically beneficial only for the no calcification group. The difference emerged as significant only for the high IIEF-EF group (≥17) in both respects and for symptom bother score in the group with no sexual activity.

Experts' comments:
CCH is an injectable proteinase that hydrolyzes collagen in its native triple-helical conformation, resulting in lysis of collagen deposits that build up in tunica albuginea of penile tissue and cause PD. CCH is the only drug approved for the treatment of PD by the US Food and Drug Administration and is indicated in the European Association of Urology 2015 guidelines with a level of evidence of 1b and grade B recommendation. This study performs the necessary subgroup data analysis to find the optimal patient group for CCH treatment and includes >800 patients, giving statistical power to the study.

The study is different from other similar studies by virtue of its larger patient population (n = 836), assessment of four subgroups, and placebo-controlled nature. Although a similar significant percentage of curvature reduction has been observed in both subgroups for the two studies, the lack of significance in bother-score reduction between CCH and placebo in the 60–90° group suggests possible unsatisfactory results for greater curvatures [1–3]. The PD questionnaire should be given importance as much as curvature degrees in the management of PD and used as guidance for assessment and follow-up of treatment [4]. Although the necessity of surgical intervention may not change after CCH administration, the choice of surgery (Nesbit vs grafting) may. A consecutive successful surgery may be performed for these patients without intraoperative difficulty, decreased penile sensitivity, or vascular deficiency [5]. However, the number of patients (n = 7) and the plausibility of post-treatment penile/intracavernous hematoma suggest the need for further studies.

This study suggests CCH primary injection as a viable option for PD patients with >2-yr onset time, 30–60° curvature, high EF capacity (IIEF-EF ≥17), and no calcification. Other studies with the sole purpose of subgroup assessment from initiation may improve on the lack of patient numbers in penile-plaque, low-EF subgroups and thus show the insignificance of CCH treatment in these groups.

Conflicts of interest: The authors have nothing to disclose.

References

Ates Kadioglu∗, Abubekir Boyuk, Emre Salabas
Section of Andrology, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey

∗Corresponding author.
E-mail address: kadiogluates@ttmail.com (A. Kadioglu).

Re: Adverse Effects of Androgen Deprivation Therapy and Strategies to Mitigate Them
Nguyen PL, Alibhai SMH, Basaria S, et al
Eur Urol 2015;67:825–36

Expert's summary:
Within a multidisciplinary framework, the authors underline that androgen deprivation therapy (ADT) is an important component of the treatment of locally advanced and metastatic prostate cancer (PCa) and that its use is associated with short- and long-term adverse effects on the health and quality of life of patients. A Medline search was conducted to identify randomized trials testing mitigation strategies to prevent or improve these side effects.

The authors carefully detail the symptoms linked to ADT, including hot flashes, impotence, fatigue, metabolic changes, anemia, gynecomastia, lower bone mineral density, muscle loss, and cardiovascular events. They also provide evidence-based recommendations for each of the symptoms that physicians should be aware of to help patients, as well as advice on diet and physical exercise.

The authors conclude that ADT should be avoided as monotherapy for localized PCa before prostatectomy and as a combination with radiation for low-risk localized PCa.

Expert's comments:
Nguyen et al provide a very comprehensive analysis that can enhance the knowledge of urologists, radiation oncologists, and medical oncologists who manage ADT. They evaluate the risk-benefit ratio for ADT and describe strategies for mitigating its side effects. These strategies require clinicians administering ADT to be aware of the comorbidities, way of life, degree of physical pain, and sexual health status of their patients, and to take time to listen to them. This holistic approach can motivate patients to help them tolerate the side effects and to make them care partners to solve difficult situations. Mitigation of side effects also requires organization