

On incidence, diagnostic algorithms and in-depth characterization of thyroid cancer

Akademisk avhandling

Som för avläggande av doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligen försvaras i Hjärtats Aula, Sahlgrenska Universitetssjukhuset, Vita Stråket 12, den 12 april 2024, klockan 9.00

av Jakob Dahlberg

Fakultetsopponent:

Professor Malin Sund

University of Helsinki, Helsinki Finland

Avhandlingen baseras på följande delarbeten

- I. Dahlberg J, Adok C, Bümbling P, Demir A, Hedbäck G, Nilsson B, Nilsson M, Jansson S. Incidence, detection and outcome of differentiated thyroid cancer in Western Sweden.
BJS Open 2021 Oct; 5(5): zrab099.
- II. Dahlberg J, Carlqvist J, Larsson E, Elias E, Muth A. Effects of implementation of EU-TIRADS risk stratification in a thyroid cancer programme in Western Sweden - a retrospective cohort study. *Submitted*.
- III. Dahlberg J, Carlqvist J, Örtoft A, Hammarstedt L, Aula E, Hellström M, Elias E, Muth A. A randomized controlled trial comparing non-selective vs selective cytology using EU-TIRADS – the Ultracyt study. *Manuscript*.
- IV. Schoultz E, Dahlberg J, Nilsson L, Karlsson J, Carlsson T, Mohammad G, Fagman H, Muth A, Elias E, Sayin V, Nilsson J, Nilsson M. Tumor cell origin and new target therapy options of squamous cell carcinoma in the thyroid.
Manuscript

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Abstract

Background: Thyroid cancer (TC) incidence has increased dramatically. Overzealous detection of subclinical disease is the most common explanation. However, whether the higher rate of diagnosis of subclinical disease might conceal a true TC increase is unknown. EU-TIRADS has been developed to guide further management of nodules. Real-world data as well as controlled trials on effect and safety are largely missing. Although overall prognosis of TC is excellent, a subgroup of patients has limited treatment options and new ones need to be developed.

Aims: The objectives of Paper I were to investigate which tumor stages of TC were increasing and the modes of detection. Paper II and II aimed at assessing the impact and safety of EU-TIRADS on nodule management. Paper IV aimed to establish PDX model of TC development and drug testing.

Methods: Paper I was a population-based study. Paper II was a single center retrospective cohort study and Paper III was a regional randomized controlled trial. Paper IV was a prospective trial collecting tumor tissues from patients with advanced TC, subsequently transplanted to immunodeficient mice.

Results: TC increased threefold during 2001-2014 in Western Sweden. The increase comprised stages T1a-T3 and the most common mode of detection was clinical symptoms, mainly a palpable tumor. Imaging did not contribute to increased TC incidence. EU-TIRADS reduced cytology by 7% without missing TC diagnosis. Comparing selective and non-selective FNA revealed that EU-TIRADS significantly reduced the frequency of unnecessary FNA. Among fresh tumor tissue samples obtained from advanced TC only squamous cell carcinoma (SCC) was successfully transplanted to immunodeficient mice. Targeted therapy based on mutation profile inhibited PDX growth.

Conclusion: Increased TC incidence in Western Sweden was due to other factors than unnecessary imaging. A true increase cannot be ruled out. EU-TIRADS does not miss TC diagnosis but has limited impact on the clinical management of thyroid nodules. A thyroid origin of SCC was documented. Novel therapeutic options were suggested arguing for global mutation analysis of all patients with anaplastic TC.

Keywords: thyroid cancer, thyroid nodule, ultrasound, ultrasonography, SCC, PDX