Objective reporting of hormone-naïve neuroendocrine cells in prostate cancer correlates with poor outcomes: A systematic review and meta-analysis.

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Introduction

A pathological variant of typical prostatic adenocarcinoma mixed with neuroendocrine cells has been previously reported (Adeno-NE). Neuroendocrine cells in Adeno-NE can only be identified through immunohistochemical staining with NE biomarkers.[1] Prevalence of this mixed pathology ranges between 10-100% of patients and the cause of this variance is unknown.[2] Due conflicting evidence on the prognostic value of Adeno-NE, there is currently no clinical recommendation to stain and risk-stratify these patients at diagnosis. However, given our contemporary understanding of Adeno-NE in more recent literature, there is value in revisiting the prognostic potential of this pathology.[3]

Aims

The aim of this study was to understand the impact of Adeno-NE in early stage prostate cancer on disease progression and survival

Methodology

Search terms: prostatic neoplasms AND neuroendocrine

Databases: Medline, CENTRAL, Biosis Previews, Embase, Scopus
<inception to 9th July 2021>

Inclusion criteria:

- ✓ Hormone-naïve prostate cancer patients
- ✓ Prostate tissue stained with one of the four main NE markers: Chromogranin A (CgA), NSE, Synaptophysin (Syn) and CD56[1]

Primary outcome measures:
Prevalence of positive staining with one or more NE markers
Secondary outcome measures:
Correlation of Adeno-NE with tumour grade, treatment failure and survival

Results

1. Objective criteria significantly reduces variation in reporting Adeno-NE

Prevalence of Adeno-NE was most accurately estimated by objective criteria at 26% (Figure 1). However, amongst studies that used objective criteria, few used the same threshold of cells.

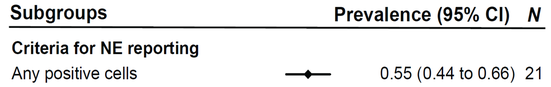

Figure 1: Subgroups of prevalence according to reporting criteria

2. Objectively scored Adeno-NE is prognostic for treatment failure and prostate cancer-specific survival.

Patients with objectively scored Adeno-NE had a 7-fold increase in risk of poorer prostate cancer-specific survival and a 2-fold increase in risk of biochemical recurrence (Figure 2).

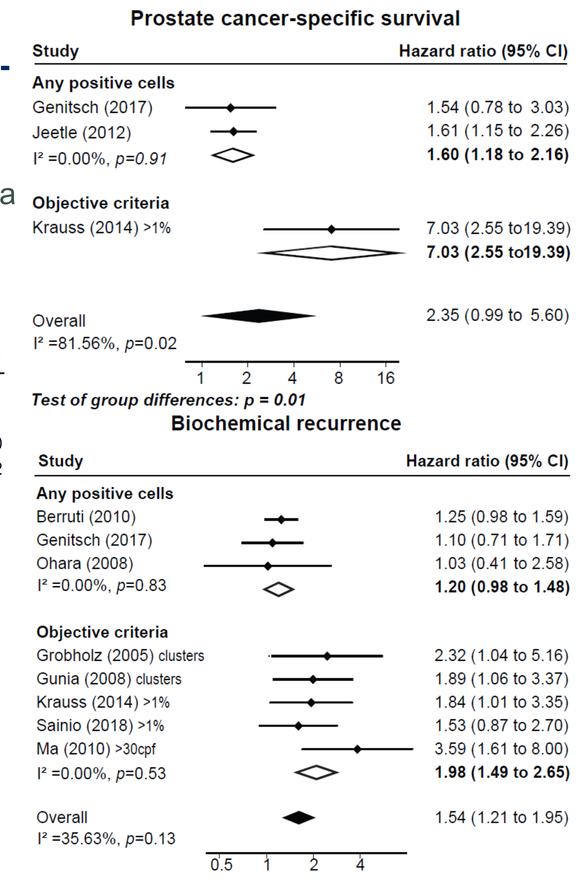

Figure 2: Clinical outcomes of patients according to reporting criteria

Conclusions

Our review found that objective reporting of Adeno-NE in hormone naïve prostate cancer correlates with poor outcomes. Improved clinical decision-making is contingent on identifying these patients at diagnosis.

[1] Epstein JI, Amin MB, Beltran H, et al. Proposed morphologic classification of prostate cancer with neuroendocrine differentiation. Am J Surg Pathol. 2014; 38:756-67
[2] Di Sant'Agnese PA. Neuroendocrine differentiation in human prostatic carcinoma. Hum Pathol. 1992; 23:287-96
[3] Beltran H, Hruszkewycz A, Scher HI, et al. The Role of Lineage Plasticity in Prostate Cancer Therapy Resistance. Clin Cancer Res 2019;25:6916-6924