

Abstract: P1610

Title: VALIDATION AND CLINICAL CHARACTERISTICS OF THROMBOTIC THROMBOCYTOPENIC PURPURA AND EVANS SYNDROME DIAGNOSES IN NATIONWIDE DANISH HEALTH REGISTERS

Abstract Type: Poster Presentation

Session Title: Platelet disorders

Background:

Early recognition and treatment of Thrombotic Thrombocytopenic Purpura (TTP) is vital for patients' prognoses. Plasma exchange (PEX) has improved survival and introduction of Rituximab has reduced risk of relapse, but patients are still susceptible to a number of complications and late effects, which are yet to be studied in depth across entire populations. While possible in Denmark due to routinely collected health data, the diagnosis has not been validated. In our own register based studies of Evans syndrome (ES), we have seen few patients diagnosed with both ES and TTP, raising concerns of diagnostic misclassification.

Aims:

We aimed to validate diagnoses of TTP and ES, and described initial treatment, complications, and health outcomes of confirmed patients.

Methods:

Patients ≥ 18 years were identified in the Danish National Registry of Patients through ICD codes indicative of TTP or Evans syndrome 2000-2019. Medical journals were reviewed and data collected by local hematologists at 9 centres.

Positive predictive values (PPV) were estimated for TTP and ES diagnosis registrations. Descriptive statistics were estimated for baseline information, initial treatment, complications, relapses and survival (follow-up until May 2022), both overall and compared for patients diagnosed 2000-2009 and 2010-2019.

Results:

In total, 355 eligible patients were identified in the nationwide register. Journal Data was available for 149 patients registered with TTP and 110 with ES. Unavailable journals were predominantly from 2000-2009. PPV was 46.3% [95%CI 38.1; 54.7] for TTP and 59.1% [49.3; 68.4] for ES, and most frequent misclassified diagnoses were cancer-associated TMA and ITP, respectively. Only 1.3% of patients registered with TTP were misclassified ES patients, and 1.8% of registered ES patients misclassified TTP patients.

For confirmed TTP patients, 79% had ADAMTS13 activity analysed. Proportion presenting with neurological symptoms was comparable from 2000-2009 to 2010-2019 (75 vs 81%), as was median duration of PEX (15 vs 13 days). Median duration of steroid course increased from 46.0 [17.5; 76.0] to 87.0 [47.5; 141.5] days ($P = 0.04$), and proportion treated with Rituximab increased from 46.2% [19.2; 74.9] to 62.1% [48.4; 74.5] ($P = 0.29$). Intensive care was required for 25 vs 28% of patients, organ failure decreased from 53.8% [25.1; 80.8] to 27.6% [16.7; 40.9] ($P = 0.07$), and CNS failure fell from 38.5% [13.9; 68.4] to 17.2% [8.6; 29.4] ($P = 0.09$). Infection occurred in 31 vs 22% of patients, and relapse in 25 vs 14%. Early mortality remained high between the two time periods (figure).

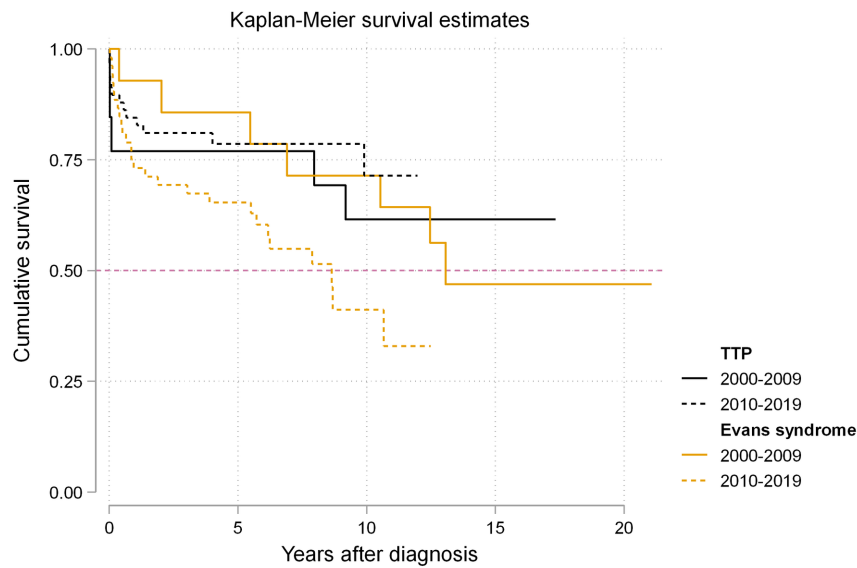
For confirmed ES patients, median duration of steroid course (days) decreased from 144.5 [30.0; 306.0] to 106.5 [42.0; 169.5] from 2000-2009 to 2010-2019 ($P = 0.24$). Rituximab use was constant at 57%, as was infection at 21%, while 33 vs 38% suffered from relapse during follow up.

Summary/Conclusion:

Register-based studies of TTP and ES should be supported with medical journal validation or other supportive

measures (e.g. ADAMTS13 data), as diagnosis code alone is unreliable, although misclassification between the two is not a concern. While no signs of reduced early mortality was observed, some acute clinical complications such as organ failure and CNS failure showed trends of improvement across study periods among TTP patients. However, analyses lacked precision. Increased measurement of ADAMTS13 activity will likely improve timely detection and treatment of more TTP patients, which continue to be a priority.

Figure: Survival of TTP and Evans syndrome patients by diagnosis period



Keywords: Autoimmune hemolytic anemia (AIHA), Clinical outcome, Thrombotic thrombocytopenic purpura (TTP), Immune thrombocytopenia (ITP)