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Population-based long-term follow-up of patients with myeloproliferative neoplasm: Complications and Prognosis.

Akademisk avhandling

Som för avläggande av medicin doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i Hörsal Arvid Carlsson, Academicum, Medicinargatan 3, Göteborg. Fredagen den 23 februari 2018, klockan 9:00.

av

Khadija Abdulkarim

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Avhandlingen baseras på följande delarbeten

I. **Abdulkarim K,** Girodon F, Johansson P, Maynadié M, Kutti J, Carli P-M, Bovet E, Andréasson B. AML transformation in 56 patients with Ph- MPD in two well defined populations. Eur J Haematol, 2009. **82**(2): p. 106-11

II. **Abdulkarim K,** Ridell B, Johansson P, Kutti J, Safai-Kutti S, Andréasson B. The impact of peripheral blood values and bone marrow findings on prognosis for patients with essential thrombocythemia and polycythemia vera. Eur J Haematol, 2011. **86**(2): p. 148-55.

III. Bonicelli G, **Abdulkarim K,** Mounier M, Johansson P, Rossi C, Jooste V, Andréasson B. Maynadié M, Girodon F. Leucocytosis and thrombosis at diagnosis are associated with poor survival in polycythaemia vera: a population-based study of 327 patients. Br J Haematol, 2013. **160**(2): p. 251-254.

IV. **Abdulkarim K,** Samuelsson J, Johansson P, Andréasson B. Risk factors for vascular complications and treatment patterns at diagnosis of 2389 PV and ET patients: Real-world data from Swedish MPN registry; Eur J Haematol,2017.98(6) p.577-583.

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Population-based long-term follow-up of patients with myeloproliferative neoplasm: complications and prognosis.

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Philadelphia chromosome negative myeloproliferative neoplasms (Ph-MPNs) are rare clonal hematological malignancies mainly, including polycythemia vera (PV), essential thrombocythemia (ET) and myelofibrosis (MF). Patients with these diseases run a high risk of vascular complications and may transform to acute myeloid leukemia (AML). Population-based studies relating to these issues are few in number.

The aims were *(i)* to investigate the rate of AML development in subtypes of Ph-MPNs, *(ii)* to determine whether clinical and bone marrow findings at diagnosis have an impact on survival and vascular complications in PV and ET, *(iii)* to find prognostic tools based on clinical findings in newly diagnosed PV and *(iv)* to describe the "real"- life data from newly diagnosed PV and ET. We have investigated these issues in population-based material; the first and the third studies were based on patients from both Gothenburg, Sweden, and the Côte d`Or area, France, and the second study was population-based from Gothenburg and the fourth study comprised PV and ET patients in the National MPN Registry.

In the median observation period of 15 years, 7% (56 of 795) of patients with Ph-MPN transformed to AML. The yearly rate of AML transformation was significantly higher in MF (1.09%) compared with that of ET (0.37%) and PV (0.38%); ($p = 0.02$ and $p = 0.002$ respectively). Patients with PV had a significantly shorter survival compared with the general Swedish population (HR 1.66; CI:(1.38-1.99); $p < 0.001$). For ET, however, the corresponding survival differences did not reach statistical significance (HR 1.23; CI:(0.97-1.51); $p = 0.089$). Low hemoglobin at the time of diagnosis predicted poor survival in ET ($p = 0.0281$) and splenomegaly predicted poor survival in PV ($p = 0.037$). Using multivariate analysis, independent risk factors at diagnosis for survival in PV patients were identified as: age > 70 years, WBC > 13×10^9/L and thrombotic events. Patients with none of these risk factors had a 10-year relative survival (RS) of 84%, compared with 59% and 26% in patients with one and two or three risk factors respectively.

In the fourth study, we showed that vascular complications preceded MPN diagnosis in 35% of ET and 37% of PV and multivariate analysis identified low hemoglobin as a risk factor for thromboembolic complications in PV ($p = 0.012$), while in ET age > 65 years, WBC > 12×10^9 /L and the presence of the JAK2 V617F mutation were independent risk factors ($p = 0.0004$, $p = 0.0038$ and $p = 0.0016$ respectively).

Keywords: essential thrombocythemia, polycythemia vera, myelofibrosis.

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