

# Evaluation of Polycythemia Vera Diagnosis and Management: Literature Review

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## Abstract

**Background:** Polycythemia vera is considered a malignant stem cell disorder and its patients usually experience troublesome symptoms and increased risk of mortality and morbidity. Appropriate diagnosis and management is cardinal in such cases to avoid disease complications and improve the patient's quality of life. **Objective:** To review the literature that discussed the evaluation and management of cases of polycythemia vera. **Method:** PubMed database was used for articles selection, and the following keys were used in the mesh ((“polycythemia vera”[Mesh]) AND (“Management” [Mesh]) OR (“Evaluation”[Mesh])). **Conclusion:** Life-expectancy in polycythemia vera is significantly lower than that of the age- and sex-matched general population. Moreover, despite polycythemia vera is considered as a malignant hematopoietic disorder, many cases do not require chemotherapy because they usually have stable and subtle clinical course. Recent recommendations suggest that all polycythemia vera patients require phlebotomy and once- or twice-daily aspirin if there are no contraindications.

**Keywords:** Polycythemia Vera, Diagnosis, Management Approach

## INTRODUCTION

Polycythemia vera is considered a malignant stem cell disorder [1]. It is characterized by erythrocytosis and mutations activation in Janus Kinase 2 (JAK2). Marrow trilineage myeloproliferation is also shown in bone marrow biopsy in polycythemia Vera cases [2]. The estimated number of cases of polycythemia vera in the USA is 100,000. They mostly face a difficult time with the troublesome symptoms of polycythemia vera and its increased risk of mortality and morbidity [3, 4]. Polycythemia vera is one of the Philadelphia chromosomes-negative myeloproliferative neoplasm similar to myelofibrosis and essential thrombocythemia [5]. In polycythemia vera, there is an excessive clonal stem-cell proliferation of red and white blood cells as well as platelets [6]. Therefore, this will lead to hyperviscosity of the blood because of the high number of red blood cells. Consequently, the risk of thrombotic formation will increase as well as the risk of mortality [7].

So, appropriate diagnosis and management are cardinal in such cases to avoid disease complications and improve the patient's quality of life. Therefore, in this article, we aimed to review the literature that discussed the evaluation and management of cases of polycythemia vera.

## METHOD:

PubMed database was used for articles selection, and the following keys were used in the mesh ((“polycythemia vera”[Mesh]) AND (“Management”[Mesh]) OR (“Evaluation”[Mesh])). In regards to the inclusion criteria, the articles were selected based on the inclusion of one of the following topics: polycythemia vera, diagnosis, and management. Exclusion criteria were all other articles that did not have one of these topics as their primary endpoint.

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## DISCUSSION:

Patients with polycythemia vera mostly face burdensome symptoms that strongly affect their quality of life. Fatigue is the most common complaint in polycythemia vera patients accounting for 88%. Around half of polycythemia vera patients may experience bone pain, night sweats, weight loss, and pruritus<sup>[8, 9]</sup>. Pruritus can be severe and appears as a generalized burning sensation or severe itching that may develop from hot weather, contact with water, or vigorous exercise. These troublesome manifestations can last for more than half an hour, which may lead the patient to aggression, irritability, and suicidal ideation<sup>[8, 10]</sup>. Moreover, splenomegaly can develop in one-third of the patients and this is considered as an indication of the severe and late stage of the disease<sup>[11]</sup>. At this stage and due to splenomegaly, polycythemia vera patients may experience a new variety of symptoms from nausea, early satiety, and abdominal pain to portal hypertension<sup>[8, 10]</sup>.

The cardinal step in managing polycythemia vera cases is confirming the diagnosis. Incorrect diagnosis will make the patient go through ineffective and sometimes harmful therapy. Diagnosis of polycythemia vera is done based on the 2016 WHO criteria and it requires either all 3 major criteria or the first 2 major criteria and the minor criterion<sup>[2]</sup>. The major criteria include first hemoglobin >16.5 g/dL in men or >16 g/dL in women or hematocrit >49% in men or > 48% in women or increased red blood cell mass. Secondly, bone marrow tri-lineage proliferation with Pleomorphic mature megakaryocytes. Thirdly, the presence of JAK2 mutation. The minor criterion is the presence of subnormal serum erythropoietin levels<sup>[12]</sup>.

Teffari *et al.*<sup>[12]</sup> provided a practical diagnostic algorithm for polycythemia vera. When polycythemia vera is suspected by high hemoglobin or high hematocrit percentage, the next step is blood JAK2 mutation screening. If it was positive, the bone marrow biopsy is advised to confirm the diagnosis and perform karyotyping. If JAK2 is negative, serum erythropoietin levels must be checked. If it was normal or elevated, it is not polycythemia vera. Nevertheless, subnormal serum erythropoietin level mandates bone marrow biopsy for further confirmation<sup>[12]</sup>.

Despite polycythemia vera is considered as a malignant hematopoietic disorder, many cases do not require chemotherapy because they usually have stable and subtle clinical course. This kind of case should be treated based on the clinical manifestations to avoid the consequences of the aggressive treatment, especially in this disease because most of the clinical manifestations develop from the overproduction of normal blood cells. Therefore, lowering the numbers aggressively is not mandatory in most of the cases<sup>[13]</sup>.

Polycythemia vera survival rates are affected by multiple factors, such as age, high leukocytes count, and thrombosis<sup>[14]</sup>. Life-expectancy in polycythemia vera is significantly

lower than that of the age- and sex-matched general population. The estimated median for polycythemia vera patients who are above 60 years old of age is 14 years, while for patients who are younger than age 60 years, the median is 24 years<sup>[14, 15]</sup>.

In addition, one of the major life-threatening complications in polycythemia vera is thrombosis, with an incidence range of 6–17% for 3 years<sup>[16, 17]</sup>. Thrombosis in polycythemia vera has several risk factors like increasing age, history of thrombosis, heart failure, high hematocrit count, smoking, and high blood pressure<sup>[18, 19]</sup>. Moreover, leukocyte count >15 × 10<sup>9</sup>/L is considered as a risk factor in polycythemia vera cases for thrombosis, especially myocardial infarction<sup>[20, 21]</sup>. Since thrombosis is the main cause of death accounting for 41%, recommendations for the management of polycythemia vera are based on thrombotic risk and how to reduce it<sup>[18]</sup>. Finazzi *et al.*<sup>[18]</sup> conducted a study on 1638 polycythemia vera patients to evaluate the role of aspirin in preventing thrombosis in such cases. 39% of the patients had a history of thrombosis from the time of diagnosis to the time of enrollment. They found that antithrombotic therapy appears to be an effective treatment in limiting the risk of thrombosis. 14% of the enrolled patients experienced thrombotic events in the 2.8 years period of follow-up with an incidence of 5.5 events/100 patients per year<sup>[18]</sup>.

Increasing rates of thrombosis events in polycythemia vera patients were correlated with increased hematocrit as one of the risk factors of thrombosis in polycythemia vera patients<sup>[21]</sup>. Marchioli *et al.*<sup>[19]</sup> in their paper compared 2 groups of polycythemia vera patients who receive treatment to maintain 2 hematocrit levels. One group received more intensive treatment to keep hematocrit below 45% (low-hematocrit group) and the other group received less intensive treatment to keep hematocrit between 45% to 50% (high-hematocrit group). The findings revealed that rates of cerebral vascular events and deep-vein thrombosis were enhanced in the high-hematocrit group. The incidence of death from cardiovascular causes or major thrombosis was 1.1 per 100 person-years in the low-hematocrit group and 4.4 per 100 person-years in the high-hematocrit group. The rate of death from cardiovascular causes or major thrombosis with keeping a hematocrit target of 45 to 50% was four times higher than with keeping a hematocrit target of less than 45%<sup>[19]</sup>.

The mainstay of therapy in lowering the hematocrit level is phlebotomy. If it is performed properly, it will prevent the major complication of polycythemia vera, which is thrombosis<sup>[22]</sup>. Recent recommendations suggest that all polycythemia vera patients require phlebotomy and once- or twice-daily aspirin if there are no contraindications<sup>[23]</sup>.

## CONCLUSION:

Life-expectancy in polycythemia vera is meaningfully lower than that of the age- and sex-matched general population. Moreover, despite polycythemia vera is considered as a malignant hematopoietic disorder, many cases do not require

chemotherapy because they usually have stable and subtle clinical course. Recent recommendations suggest that all polycythemia vera patients require phlebotomy and once- or twice-daily aspirin to prevent serious complications.

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