# Potential Effect of Antiplatelet and Anticoagulant Therapy on the Timing of the Diagnosis of Bladder Cancer

Marco Moschini,[1,2,3] R. Jeffrey Karnes,[3] Nazareno Suardi,[1] Marco Bianchi,[1] Federico Pellucchi,[4] Lorenzo Rocchini,[4] Rocco Damiano,[2] Vincenzo Serretta,[5] Andrea Salonia,[1] Francesco Montorsi,[1] Alberto Briganti,[1] Renzo Colombo[1]

## Abstract

**The most common presenting symptom of bladder cancer (BCa) is hematuria. However, the use of antiplatelet or anticoagulant therapy (AAT) is increasing. We report for the first time in published studies that patients diagnosed with BCa at an emergency room visit for an episode of macroscopic hematuria will have a lower tumor grade and stage if they were receiving AAT during the hematuria event.**

**Background:** The most common presenting symptom of bladder cancer (BCa) is hematuria. The present study was designed to define whether patients taking antiplatelet and/or anticoagulant drugs might experience hematuria at an earlier stage or grade of BCa. **Patients and Methods:** The data from 1532 consecutive patients who presented to the emergency unit of our institute from 2004 to 2012 because of gross hematuria as a single symptom were evaluated. Patients (n = 227) with a further diagnosis of BCa were included in our study. For the purpose of the present study, patients were divided into 2 groups: patients receiving antiplatelet or anticoagulant therapy (AAT) (group 1) and patients not receiving AAT (group 2) at the moment of the macroscopic hematuria episode. The effect of AAT on the pathologic stage and grade of BCa was statistically assessed using univariate and multivariate logistic regression analysis. **Results:** A total of 59 (26%) and 168 (74%) patients were included in groups 1 and 2, respectively. On multivariate logistic regression analysis, ATT conferred a protective effect against both pathologic stage ≥ T2 (odds ratio [OR], 0.37; 95% confidential interval [CI], 0.12-0.66; $P = .01$) and higher grade (OR, 0.56; 95% CI, 0.26-0.85; $P = .02$) at tumor presentation. **Conclusion:** According to the results of the present retrospective investigation, patients who received AAT seem to experience gross hematuria significantly earlier than do untreated patients, resulting in the chance of an earlier diagnosis and treatment of bladder cancer.

*Clinical Genitourinary Cancer,* Vol. 14, No. 3, e245-50 
**Keywords:** Anticoagulant, Antiplatelet, Bladder cancer, Emergency room, Hematuria, Non-muscle invasive bladder cancer

## Introduction

Bladder cancer (BCa) represents the fifth most commonly diagnosed tumor in the Western world and the second most diagnosed genitourinary cancer.[1] Despite the high proportion of patients diagnosed with non-muscle invasive disease, roughly 25% of overall patients will have locally advanced or metastatic cancer at tumor presentation.[2] Although microhematuria, dysuria, flank pain, and constitutional symptoms are well-recognized as being related to bladder cancer, almost all patients are diagnosed after a single episode of macroscopic hematuria.[3] However, although macroscopic hematuria has long been assumed to be the earliest and most frequent symptom of BCa,[4] its effect on current urologic practice deserves better investigation because of some novel epidemiologic and clinical findings.

[1]Department of Urology, Urological Research Institute, Vita-Salute San Raffaele University, San Raffaele Scientific Institute, Milan, Italy
[2]Doctorate Research Program, Magna Graecia University of Catanzaro, Catanzaro, Italy
[3]Department of Urology, Mayo Clinic, Rochester, MN
[4]Department of Urology, Papa Giovanni XXIII Hospital, Bergamo, Italy
[5]Dipartimento di Discipline Chirurgiche ed Oncologiche, Università degli Studi di Palermo, Palermo, Italy

Submitted: Jul 7, 2015; Revised: Jul 30, 2015; Accepted: Aug 8, 2015; Epub: Aug 18, 2015

Address for correspondence: Marco Moschini, MD, Department of Urology, Vita-Salute San Raffaele University, San Raffaele Hospital, Via Olgettina, Milan 60-20132, Italy
E-mail contact: marco.moschini87@gmail.com

1558-7673/$ - see frontmatter 
http://dx.doi.org/10.1016/j.clgc.2015.08.003

Antiplatelet and/or anticoagulant therapy (AAT), for example, represents one of the most widely used long-lasting treatments of both primary and secondary cardiovascular risk factors.[5,6] Percutaneous intervention with coronary stent implantation in patients with coronary artery disease has dramatically increased worldwide, requiring prolonged single or dual antiplatelet therapy. Likewise, the use of oral anticoagulation drugs for the prevention and treatment of deep vein thrombosis and atrial fibrillation has greatly increased in the past 2 decades. However, old age and smoking habits are well-known risk factors common to both cardiovascular diseases and bladder cancer.[2,7] Thus, we hypothesized that patients with BCa and undergoing chronic treatment with AAT might experience macroscopic hematuria earlier than patients with undiagnosed BCa who have never received AAT.

## Patients and Methods

### *Study Population and Clinical and Pathologic Evaluation*

After institutional review board approval, we evaluated 1532 consecutive patients who presented from January 2004 to December 2012 at the emergency room (ER) of a single tertiary referral center because of an episode of macroscopic hematuria. All the included patients provided informed consent for the use of their

**Table 1** Demographic and Pathologic Data of Patients, Stratified by Antiplatelet or Anticoagulant Therapy Use

| Variable | Overall (n = 227, 100%) | No AAT (n = 168, 74%) | AAT (n = 59, 26%) | *P* Value |
|---|---|---|---|---|
| Age (years) | | | | <.01 |
| Mean | 67.2 | 65.6 | 71.7 | |
| Median | 68.7 | 65.8 | 73.1 | |
| IQR | 59.1-75.5 | 57.7-74.8 | 65.0-79.2 | |
| Charlson comorbidity score | | | | .001 |
| 0 | 73 (32.2) | 62 (37.1) | 11 (18.3) | |
| 1 | 146 (64.3) | 103 (61.7) | 43 (71.7) | |
| ≥2 | 8 (3.5) | 2 (1.2) | 6 (10.0) | |
| Tumor focality | | | | .3 |
| Single | 112 (49.5) | 80 (47.5) | 31 (52.9) | |
| Multiple | 115 (50.5) | 88 (52.5) | 28 (47.1) | |
| Smoking habits | | | | .02 |
| Actual smoker | 62 (27.5) | 44 (26.2) | 9 (15.2) | |
| Former | 97 (42.8) | 66 (39.3) | 31 (52.5) | |
| No | 68 (29.7) | 58 (34.5) | 19 (32.2) | |
| Lifetime cumulative smoking exposure | | | | .04 |
| None | 68 (29.7) | 58 (34.5) | 10 (16.9) | |
| Light, short term | 50 (21.8) | 39 (23.2) | 11 (18.6) | |
| Heavy, short term | 50 (21.8) | 32 (19.0) | 18 (30.5) | |
| Light, long term | 38 (16.6) | 25 (14.9) | 13 (22.0) | |
| Heavy, long term | 21 (9.2) | 14 (8.3) | 7 (11.8) | |
| Sex | | | | .1 |
| Female | 40 (17.6) | 34 (20.2) | 6 (10.2) | |
| Male | 187 (82.4) | 134 (69.8) | 53 (89.8) | |
| Tumor size >3 mm | 83 (36.5) | 88 (52.2) | 17 (29.4) | .01 |
| CIS (%) | 22 (9.7) | 19 (11.3) | 3 (5.1) | .1 |
| Tumor grade (WHO 1973) | | | | .004 |
| 1 | 12 (4.0) | 10 (4.8) | 2 (1.7) | |
| 2 | 60 (26.8) | 35 (21.1) | 25 (43.1) | |
| 3 | 155 (69.2) | 123 (74.1) | 32 (55.2) | |
| Overall grade (WHO 2004) | | | | .01 |
| Low | 54 (24.1) | 34 (20.5) | 20 (34.5) | |
| High | 170 (75.9) | 134 (79.5) | 39 (65.5) | |
| Pathologic stage | | | | .01 |
| pTa-pT1 | 107 (47.1) | 72 (42.9) | 35 (59.3) | |
| pT2 | 120 (52.9) | 96 (57.1) | 24 (40.7) | |

Data presented as n (%).
Abbreviations: AAT = antiplatelet or anticoagulant therapies; IQR = interquartile range; WHO = World Health Organization.