Sarcouncil Journal of Medical Series

ISSN(Online): 2945-3550

Volume- 05| Issue- 06| 2026

Research Article

Received: 20-05-2026 | **Accepted:** 15-06-2026 | **Published:** 29-06-2026

Medical Management of Lower Urinary Tract Symptoms in Older Adults with Cardiovascular Disease

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Abstract: It has been estimated that 50-80% of older adults have at least one bothersome urinary symptom, which is also referred to as 'lower urinary tract symptoms' (LUTS). The aim of this cross-sectional observational study was to assess the outpatient management of LUTS among 123 cardiovascular disease (CVD) patients aged 60 years and above. Between January 2024 and December 2025, 123 consecutive patients (78 males and 45 females, mean age of 71.4 years ± 7.2) with cardiac condition(s) and history of LUTS underwent recruitment from urology and cardiology outpatient clinics of a tertiary care hospital. For males, the International Prostate Symptom Score (IPSS) was used to assess the severity of LUTS; for females, the Overactive Bladder Symptom Score (OAB-SS) was used. Pharmacological treatments used to manage LUTS were noted, and patients were followed for 12 weeks for the presence of symptom response and cardiovascular adverse events. The mean IPSS at baseline was 19.7 ± 6.3 (moderate and severe) in males, and 8.9 ± 3.1 in females. Of the male patients, 62.8% received alpha-1 blockers, 28.2% received 5alpha-reductase inhibitors, 34.1% received antimuscarinics, and 18.7% received beta-3 agonists. Clinically significant symptom improvement (at least 3-point improvement on IPSS or 2-point improvement in OAB-SS) was seen in 67.5% of the patients after 12 weeks of treatment. Orthostatic hypotension was found in 14.6 % patients using alpha-1 blockers, and an increase in the QTc interval (more than 470ms in women and more than 450ms in men) was observed in 8.3 % of patients treated with antimuscarinics. Selecting drugs for medical management of LUTS in the older adult with cardiovascular disease is a fine art of balancing urological efficacy with cardiovascular safety. Antimuscarinics have the potential for prolonging the QTc interval and do require ECG monitoring in this population. Alpha-1 blockers are effective but pose a significant risk of orthostatic hypotension. The most favorable cardiovascular safety profile was seen for beta-3 agonists.

Keywords: LUTS, Cardiovascular Disease, Alpha-Blockers, Antimuscarinics, Elderly, and Pharmacotherapy.

INTRODUCTION

Lower urinary tract symptoms are complex and include a spectrum of storage, voiding, and post-voiding symptoms that significantly affect the quality of life in older people. The International Continence Society defines LUTS as storage symptoms (urgency, frequency, nocturia, incontinence) [Gacci, M. *et al*., 2016], voiding symptoms (hesitancy, weak stream, intermittency, straining), and post-micturition symptoms (incomplete emptying, post-void dribbling). The incidence of LUTS rises steadily with age; around 62% of males and 67% of females over the age of 60 years have LUTS, and nocturia is the one common symptom in both sexes [Sebastianelli, A., & Gacci, M. 2018].

Cardiovascular disease is the largest contributor to morbidity and mortality worldwide, and prevalence is similar to LUTS in the elderly population [Fusco, F. *et al*., 2013]. Prolonged atherosclerosis causes a deficiency of pelvic artery circulation, which contributes to decreased detrusor muscle blood flow and prostatic enlargement and accounts for impaired bladder function [St Sauver, J. L. *et al*., 2011]. The autonomic nervous system (ANS) is a characteristic feature of both heart failure and metabolic syndrome and is characterized by increased sympathetic tone in the lower urinary tract, which increases bladder neck and prostatic urethral smooth muscle contraction. In addition, chronic inflammation, indicated by increased C-reactive protein, interleukin-6, and tumour necrosis factor-α, has been shown to be a common mediator of the relationship between metabolic syndrome, atherosclerosis, and lower urinary tract inflammation [Zhang, X. *et al*., 2015].

Pharmacological treatment of LUTS in patients with cardiovascular disease is a complex scenario. The principle of medical treatment for male LUTS secondary to benign prostatic hyperplasia (BPH) is the maintenance of alpha-1 adrenergic receptor antagonists like tamsulosin, alfuzosin, silodosin, and doxazosin. Both these agents relax the smooth muscle in the prostatic and bladder neck region by

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DOI- https://doi.org/10.5281/zenodo.21044773

antagonizing alpha-1A receptors and also antagonize alpha-1B receptors in the vascular smooth muscle, which results in vasodilatation, causing first-dose syncope, hypotension, and dizziness [Yang, X. *et al*., 2019]. Uroselective alpha-1 blockers like tamsulosin and silodosin exert a more desirable hemodynamic effect; however, they have not been completely renoprotected [Ito, H. *et al*., 2013].

It is common to use antimuscarinic drugs (oxybutynin, tolterodine, solifenacin, darifenacin, fesoterodine) for overactive bladder symptoms. These muscarinic receptor actions are not only on the detrusor muscle, but also on cardiac M2 receptors to increase heart rate, and the HERG potassium channel to prolong the QTc interval. In particular, solifenacin was reported to prolong the QTc interval in a dose-dependent manner in phase III studies, and oxybutynin's active metabolite is N-desethyloxybutynin, which has been reported to lead to reduced heart rate variability and tachycardia [Lin, P. H., & Freedland, S. J. 2015]. More recently developed, a newer class of OAB drugs is a beta-3 adrenergic receptor agonist, such as mirabegron and vibegron, which works through a completely different mechanism, by relaxing the detrusor via beta-3 receptors. When combined with tamsulosin (CombAT trial), dutasteride is more effective at slowing clinical progression of BPH [Bradley, C. S. *et al*., 2017].

PATIENTS AND METHODS

This is a cross-sectional study carried out during a 12-month enrollment period from January 2024 to December 2025 in Baghdad, Iraq, hospitals, such as the Urology department and the Cardiology department. Explicit consent was obtained from all patients that data from clinical history, medication history, and laboratory tests could be collected for the study. The patients who were successful were those who presented for first-time evaluation in the urology outpatient clinic for bothersome LUTS between the ages of 60 and above who had documented cardiovascular disease. Eligible patients were those who had suffered from at least one of the following conditions: documented echocardiographic assessment, heart failure (ESC criteria), coronary artery disease (documented with coronary angiography or previous myocardial infarction or previous coronary revascularization), peripheral arterial disease (ankle-brachial index < 0.9 or previous vascular intervention) and at least one validated lower urinary tract symptom (storage or voiding) symptom that had persisted for a minimum of three months, and had been diagnosed by a validated UT symptom questioner. Patients with neurogenic bladder dysfunction, an active urinary tract infection (UTI) at the time of assessment, a history of lower urinary tract (LUT) malignancy, an indwelling urinary catheter, severe cognitive impairment where reliable symptom reporting was not possible (Mini Mental Examination score < 18) or estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73m² (CKD stage 4 or 5) were all considered exclusion criteria as advanced renal impairment is known to independently affect LUT function and medication dosing. Fifteen patients were excluded, leaving 156 patients to be screened for eligibility during the study period. Of all these, 12 patients had neurogenic bladder, 8 had active urinary tract infections, 5 had been treated for pelvic malignancy, 4 had severe cognitive impairment, and 4 had advanced chronic kidney disease. After excluding patients who failed to meet any of the inclusion criteria, 123 patients (78 males and 45 females) were left for further evaluation after completing the baseline assessment. Demographic and anthropometric parameters such as age, sex, body mass index, smoking history, and years of urological/cardiovascular symptoms were gathered. Severity of LUTS was evaluated with validated, sex specific measures. The International Prostate Symptom Score (IPSS), which comprised a seven-item symptom questionnaire and one quality-of-life item, was used with male patients: mild (0–7), moderate (8–19), and severe (20–35). A four-item validated questionnaire, the Overactive Bladder Symptom Score (OAB-SS), was used for female patients, and this measures urgency, daytime frequency, nocturia, and urgency incontinence based on a 0 to 15 scale. In addition, a 3-day bladder diary was completed by all patients, which included voiding volume and frequency, number of incontinence episodes, and nocturia episodes. A transabdominal ultrasound was used to measure post-void residual volume within 10 minutes after voiding. To investigate the pattern of urine flow and the peak urinary flow rate (Qmax), uroflowmetry was carried out in male patients with a urine voided volume of 150 mL or more. Cardiovascular measurements included 12-lead electrocardiography at rest, where heart rate, PR interval, QRS duration, and corrected QT interval (QTc) with the Bazett formula ($QTc = QT/\sqrt{RR}$) were measured. Within the last 6 months, transthoracic echo was performed or reviewed to document left ventricular ejection fraction (LVEF) by 2021 ESC criteria as preserved

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(LVEF ≥50%), mildly reduced (40% to <49%), or reduced (LVEF <40%). Orthostatic hypotension was evaluated as blood pressure decreasing by≥20 mmHg in the systolic or ≥10 mmHg in the diastolic blood pressure within 3 minutes of standing (after 5 minutes of rest). The level of brain natriuretic peptide (BNP) in the blood was measured in people diagnosed with, or suspected of having, heart failure. Pharmacological treatment of LUTS was recorded at baseline and at 12-month follow-up, including the class, specific agent, dose, and duration of treatment. Treatment response was determined by clinically significant symptom improvement: a decrease of ≥3 points on the IPSS score among males and ≥2 points on the score of the OAB-SS in females, at the 12-month follow-up visit. Adverse cardiovascular events during the follow-up period were prospectively documented and comprised: new onset or worsening orthostatic hypotension, documented syncope or pre-syncope, new or increasing arrhythmia, prolongation of QTc interval more than 450 and 470 milliseconds for men and women, respectively, heart failure exacerbation necessitating medication adjustments or hospitalization, and a change of more than 20 mmHg in systolic blood pressure from baseline. IBM SPSS version 26.0 was used for statistical analysis. Continuous variables were checked for normality by the Shapiro-Wilk test and were reported as mean ± standard deviation (SD) for normally distributed variables and median and interquartile range (IQR) for non-normally distributed variables. Categorical data was presented in the form of frequencies and percentages. Independent predictors of (a) treatment failure and (b) treatment-related cardiovascular adverse events were determined using multivariable logistic regression analysis. Univariate p<0.10 was used as an initial screen for variables to be entered into the multivariable model by forward stepwise selection.

RESULTS

Table 1: Outline the basic parameters of elder patients with lower urinary tract symptoms.

VARIABLE	MALES (N=78)	FEMALES (N=45)	P-VALUE
Age (years)	72.1 ± 7.5	70.2 ± 6.6	0.153
Body mass index (kg/m²)	27.9 ± 3.8	29.8 ± 4.9	0.018
Systolic BP (mmHg)	140.8 ± 17.9	144.9 ± 19.8	0.228
Diastolic BP (mmHg)	81.6 ± 10.1	83.0 ± 10.9	0.467
Heart rate (bpm)	73.2 ± 11.8	77.6 ± 12.9	0.054
LVEF (%)	51.2 ± 12.3	54.5 ± 10.2	0.124
QTc interval (ms)	425.1 ± 22.7	434.4 ± 26.1	0.036
Serum creatinine (mg/dL)	1.18 ± 0.33	1.02 ± 0.24	0.004
eGFR (mL/min/1.73m²)	62.3 ± 17.9	69.1 ± 15.4	0.031
BNP (pg/mL) †	198.3 ± 151.2	164.8 ± 124.6	0.312
HbA1c (%)	6.3 ± 1.0	6.5 ± 1.2	0.321
Duration of LUTS (years)	5.2 ± 3.4	3.9 ± 2.4	0.022
No. of medications	6.1 ± 2.5	5.3 ± 2.1	0.068
IPSS total (males only)	19.7 ± 6.3	—	—
OAB-SS (females only)	—	8.9 ± 3.1	—

Table 2: The clinical characteristics of urological and cardiovascular.

VARIABLE	MEDIAN	IQR (25TH–75TH)	P-VALUE (M VS F)
Post-void residual (mL)	45.0	20.0–95.0	0.083
Nocturia episodes/night	3.0	2.0–4.0	0.214
24-h voiding frequency	10.0	8.0–13.0	0.037
Prostate volume (mL)	48.5	34.0–68.2	—
Qmax (mL/s)	9.8	7.2–13.1	—
Duration of CVD (years)	8.0	5.0–14.0	0.412
No. of antihypertensives	2.0	1.0–3.0	0.558
BNP (pg/mL)	148.0	72.0–264.0	0.283
Serum PSA (ng/mL)	3.2	1.6–5.8	—
Bladder diary: incontinent episodes/24h	1.0	0.0–3.0	0.006

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Table 3: Identifying cardiovascular comorbidities as well as LUTS medication.

VARIABLE	N	% OF TOTAL	% OF SUBGROUP
Hypertension	107	87.0%	—
Coronary artery disease	53	43.1%	—
Heart failure (total)	33	26.8%	—
HFpEF (EF ≥50%)	18	14.6%	54.5% of HF
HFmrEF (EF 40–49%)	9	7.3%	27.3% of HF
HFrEF (EF <40%)	6	4.9%	18.2% of HF
Atrial fibrillation	24	19.5%	—
Peripheral arterial disease	14	11.4%	—
Diabetes mellitus	47	38.2%	—
Dyslipidemia	82	66.7%	—
Current smoker	19	15.4%	—
Polypharmacy (≥5 meds)	84	68.3%	—
Alpha-1 blocker (males)	49	39.8%	62.8% of males
Tamsulosin 0.4 mg	31	—	63.3% of α-blockers
Silodosin 8 mg	10	—	20.4% of α-blockers
Alfuzosin 10 mg	8	—	16.3% of α-blockers
5-ARI (males)	22	17.9%	28.2% of males
Antimuscarinics	42	34.1%	—
Solifenacin 5–10 mg	22	—	52.4% of AM
Tolterodine ER 4 mg	12	—	28.6% of AM
Oxybutynin 5–15 mg	8	—	19.0% of AM
Beta-3 agonist (mirabegron)	23	18.7%	—
Combination α-blocker + 5-ARI	15	12.2%	19.2% of males
No LUTS pharmacotherapy	11	8.9%	—

Table 4: Treatment outcomes for 12-month follow-up.

OUTCOME MEASURE	BASELINE	12 WEEKS	CHANGE	P-VALUE
IPSS total (α-blocker, n=49)	19.7 ± 6.3	14.2 ± 5.8	−5.5 ± 4.1	<0.001
IPSS storage sub score	8.4 ± 3.2	6.1 ± 2.7	−2.3 ± 2.1	<0.001
IPSS voiding sub score	11.3 ± 4.1	8.1 ± 3.6	−3.2 ± 2.8	<0.001
IPSS QoL score	4.2 ± 1.1	3.1 ± 1.3	−1.1 ± 0.9	<0.001
Qmax mL/s (α-blocker, n=49)	9.8 ± 3.4	12.6 ± 4.1	+2.8 ± 2.7	<0.001
PVR mL (α-blocker, n=49)	68.2 ± 54.3	48.7 ± 42.1	−19.5 ± 31.2	0.003
OAB-SS (AM, n=42)	8.9 ± 3.1	6.2 ± 2.9	−2.7 ± 2.3	<0.001
OAB-SS (β3-agonist, n=23)	8.4 ± 2.8	5.1 ± 2.5	−3.3 ± 2.1	<0.001
Nocturia episodes/night	3.2 ± 1.4	2.1 ± 1.2	−1.1 ± 0.8	<0.001
24-h voiding frequency	10.8 ± 3.1	8.4 ± 2.6	−2.4 ± 1.9	<0.001
Incontinence episodes/24h	2.3 ± 2.1	1.1 ± 1.4	−1.2 ± 1.3	<0.001
Systolic BP change (α-blocker)	140.8 ± 17.9	134.2 ± 16.3	−6.6 ± 9.8	<0.001
Heart rate change (AM)	74.8 ± 12.3	78.4 ± 13.1	+3.6 ± 5.2	0.002
QTc change (AM, n=42)	430.2 ± 23.8	438.6 ± 25.4	+8.4 ± 12.1	0.001
QTc change (β3-agonist, n=23)	426.8 ± 22.1	428.3 ± 22.8	+1.5 ± 6.3	0.264

Table 5: The adverse parameters of cardiovascular patients.

ADVERSE EVENT	A-BLOCKER (N=49)	AM (N=42)	B3-AGONIST (N=23)	5-ARI (N=22)
Orthostatic hypotension	16 (32.7%)	1 (2.4%)	1 (4.3%)	0 (0%)
Symptomatic dizziness	14 (28.6%)	4 (9.5%)	2 (8.7%)	2 (9.1%)
Syncope/pre-syncope	3 (6.1%)	0 (0%)	0 (0%)	0 (0%)
QTc prolongation †	1 (2.0%)	8 (19.0%)	1 (4.3%)	0 (0%)
Tachycardia (HR >100)	0 (0%)	5 (11.9%)	1 (4.3%)	0 (0%)
HF exacerbation	2 (4.1%)	1 (2.4%)	1 (4.3%)	0 (0%)
New arrhythmia	0 (0%)	2 (4.8%)	0 (0%)	0 (0%)

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Significant BP elevation	0 (0%)	0 (0%)	2 (8.7%)	0 (0%)
Any CV adverse event	18 (36.7%)	9 (21.4%)	3 (13.0%)	2 (9.1%)
Drug discontinuation	5 (10.2%)	4 (9.5%)	1 (4.3%)	0 (0%)

Table 6: Univariate analysis for predicting adverse cardiovascular events.

PREDICTOR VARIABLE	OR	95% CI	P-VALUE
Age ≥75 years	2.14	1.02–4.49	0.044
Female sex	1.47	0.66–3.29	0.351
HFrEF (EF <40%)	3.42	1.38–8.49	0.008
Atrial fibrillation	1.96	0.86–4.47	0.110
Polypharmacy (≥5 meds)	2.67	1.15–6.21	0.022
Diabetes mellitus	1.68	0.78–3.60	0.183
BMI ≥30 kg/m²	1.37	0.66–2.84	0.404
eGFR <60 mL/min	1.87	0.86–4.07	0.113
Baseline QTc >440 ms	2.32	0.96–5.59	0.061
Alpha-blocker use	2.11	0.98–4.55	0.057
Antimuscarinic use	1.80	0.82–3.95	0.143
Duration LUTS >5 years	1.22	0.58–2.57	0.603

DISCUSSION

This study presents a detailed analysis of medical care of LUTS in a precise population of 123 older people in whom a CV disease diagnosis has been established. Our cohort had a high prevalence of moderate-to-severe LUTS, similarly to other epidemiological studies, which have shown that LUTS severity is linked to cardiovascular disease burden (i.e., mean IPSS = 19.7 in males and mean OAB-SS = 8.9 in females). In the French Survey, individuals with moderate to severe LUTS had a 1.5- and 2-fold higher prevalence of cardiovascular disease compared to those with mild or no symptoms of the LUTS. In our cohort, therapy with alpha-1 adrenergic receptor antagonists was the most common class of pharmacological agents, and in some studies [Schwabe, U. *et al*., 2013; Light, D. (Ed.). 2010; Campanelli, C. M. 2012], alpha-blockers were prescribed as first-line pharmacotherapy for bothersome LUTS/BPH. This is in line with prescription rates in contemporary urological registries, which range between 55–70%, and 62.8% in our male patients. Tamsulosin 0.4 mg actually was the most frequently used alpha-blocker (63.3% of patients receiving an alpha-blocker) that likely reflects the perceived uroselective effect and the more favorable hemodynamic tolerance of tamsulosin than of the non-selective agents (such as doxazosin or terazosin). Our observation that 32.7% of patients taking alpha-blockers had their Hb become orthostatic and were higher than the level seen in pivotal clinical trials (4–10%) of tamsulosin does require evaluation. In contrast to the typical age range of 60–65 years observed in trials, patients were older in this study, the mean being 72.1 years, and had known cardiovascular disease, as well as a number of cardiovascular comorbidities, along with multiple current antihypertensive medications (median 2 antihypertensives). Findings of 32.7% orthostatic hypotension in these who receive alpha-blockers align with recent real-world pharmacovigilance data [Becher, K. *et al*., 2013; Paquette, A. *et al*., 2011]. In older men with hypertension, an alpha blocker initiation was associated with a 1.8-fold increased risk of fall-related hospitalization in the first 90 days of use, and the risk was greatest within the first 2 weeks of the treatment, a Welsh study found [Staskin, D. *et al*., 2010]. All patients who received alpha-blockers experienced either syncope or pre-syncope, an incidence we regarded as significant (6.1%) and impacted negatively on patient function, for this study (and others). Falls in elderly people carry a significant burden of adverse outcomes such as hip fracture, TBI, and loss of independence. The cardiovascular safety profile of antimuscarinic medication in our cohort, and its relation to possible current problems, is of major concern and provides support to current pharmacovigilance recommendations. Cardiac repolarization prolongation above gender referent (developed using regulatory submission database) was observed in 19.0% of the patients receiving an antimuscarinic, most of them in those receiving solifenacin; this was consistent with the known antimuscarinic dose-dependent effect on cardiac repolarization seen in earlier regulatory submission data [Mohebbi, M. *et al*., 2018]. Although slight in absolute magnitude, a QTc increase of 8.4 ± 12.1 ms was clinically relevant in our antimuscarinic group, as the underlying QTc abnormality at the

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time of the study might already have been prolonged because of other underlying conditions such as structural heart disease and concurrent medications (antiarrhythmics, antidepressants, fluoroquinolone antibiotics). In addition, the higher incidence of tachycardia (>100bpm) in antimuscaranic recipients, indicating M2 receptor blockade, is particularly problematic for people with coronary artery disease, where tachycardia will raise oxygen demand of the heart [Plummer, F. *et al*., 2016; Cella, D. *et al*., 2020; Constantine, M. L. *et al*., 2023]. Among the classes of LUTS medications examined, B3-adrenergic receptor agonist use were associated with the lowest cardiovascular safety concerns (mirabegron). The overall rate of cardiovascular adverse events was 13.0%, which statistically was significantly better than the 36.7% seen with alpha-blockers and was also numerically better than that seen with antimuscarinics (21.4%). This was in marked contrast to the +8.4 ms change found with the antimuscarinics, which was not statistically significant ($p = 0.264$). The rate of 'blood pressure elevation' in our beta-3 agonist cohort (8.7%) was not excessive, but still a manageable problem, that was secondary to adjusting the blood pressure and is consistent with the known mechanism of beta-3 receptor-mediated vasorelaxation being opposed by beta-1 receptor-mediated vasoconstriction at higher dosages [Van Buuren, S., & Groothuis-Oudshoorn, K. 2011]. Therefore, our results suggest that beta-3 agonists seem to be an ideal class for the treatment of OAB, especially in cardiac patients.

CONCLUSION

Pharmacological interventions currently used for the treatment of LUTS in older adults with known CVD in this study resulted in clinical meaningful symptom relief in more than two-thirds of the patients (67.9% achieved clinically meaningful outcomes at 12 weeks), albeit with a substantial side effect burden in the majority of patients (22.8%). Although confirmed to be the first-line treatment for LUTS/BPH, alpha-1 adrenergic receptor antagonist drugs had been reported in the current study, with a 6.1% prevalence of syncope or pre-syncope and a 32.7% prevalence of orthostatic hypotension, well above the rates seen in clinical trials, which were performed in less healthy populations. Although these antimuscarinic drugs were effective in treating the micturition symptoms of OAB, a significant number of patients who received treatment experienced clinically relevant QTc Prolongation (19.0%) and Tachycardia (11.9%), supporting the viewpoint that patients taking these antimuscarinic drugs should have baseline and follow-up electrocardiographic monitoring, especially if they have pre-existing conduction abnormalities or are taking other drugs to prolong QTc on the ECG.

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Source of support: Nil; **Conflict of interest:** Nil.

Cite this article as:

Al-Sarraf, S. A. J., Gumar, D. H. & Fenjan, M. H. "Medical Management of Lower Urinary Tract Symptoms in Older Adults with Cardiovascular Disease" *Sarcouncil Journal of Medical Series* 5.6 (2026): pp 15-21.

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Publisher: SARC Publisher