Benefits and Risks of In-Hospital Titration of Antihypertensive Medications post-Acute Coronary Syndrome (BRIHT-AIMS-ACS) Study

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Background

- Beta-Blockers (BB), Angiotensin Converting Enzyme Inhibitors (ACEI), and Angiotensin Receptor Blockers (ARB) titrated to target doses reduce mortality and re-infarction rates after acute coronary syndromes (ACS)
- BB, ACEI, and ARB doses post-ACS at hospital discharge are lower than goal target doses associated with mortality benefit
- BB, ACEI, and ARB doses are rarely titrated to target doses in the community
- Clinical trials utilized different titration regimens with no consistent method
- Research addressing safety and effectiveness of BB, ACEI, and ARB titration regimens in the hospital setting is scarce

Objectives

Efficacy

- To determine incidence of in-hospital BB/ACEI/ARB rapid titration post-ACS
- To determine incidence of BB/ACEI/ARB target dose attainment due to rapid titration

Safety

- To describe incidence of BB/ACEI/ARB dose reductions or discontinuations early after hospital discharge post-ACS
- To describe frequency of the following ADRs early after discharge post-ACS: fatigue, fainting, dizziness, headache, insomnia, dyspnea, dry cough
- To describe the impact of ADRs on medication discontinuation rates

Methods

Design, Setting, and Sampling

- Prospective, multicenter, observational study
- In-patient cardiology wards at Kelowna General and Royal Inland Hospital
- Time-period based, consecutive sampling

Inclusion Criteria

- Hospital discharge diagnosis of ACS managed medically or with PCI
- Received BB and/or ACEI/ARB for post-ACS care. Some examples include:
  - **BB:** metoprolol, bisoprolol, carvedilol, atenolol
  - **ACEI:** ramipril, perindopril, trandolapril, captopril
  - **ARB:** valsartan, candesartan

Exclusion Criteria

- Received target doses of both BB and ACEI/ARB before enrollment
- Discharge to a skilled nursing/long-term care facility or other hospital
- Received home medication assistance

Data Collection

- Case-record form (in-hospital) & telephone questionnaire (post-discharge)

Outcomes - Efficacy

- % of patients rapidly titrated on BB/ACEI/ARB before hospital discharge
- % of patients rapidly titrated on BB/ACEI/ARB who attained target doses at 2-weeks post-discharge

Outcomes – Safety

- % of patients with BB/ACEI/ARB dose reductions or discontinuations at 2-weeks post-discharge
- % of patients who reported selected ADRs at 2-weeks post-discharge

Statistical Analysis

- Descriptive statistics using SPSS and Microsoft Excel

Definitions

- Rapid Titration: received ≥ 1 dose escalation within 72 hours of first dose OR received a moderate to high initial dose

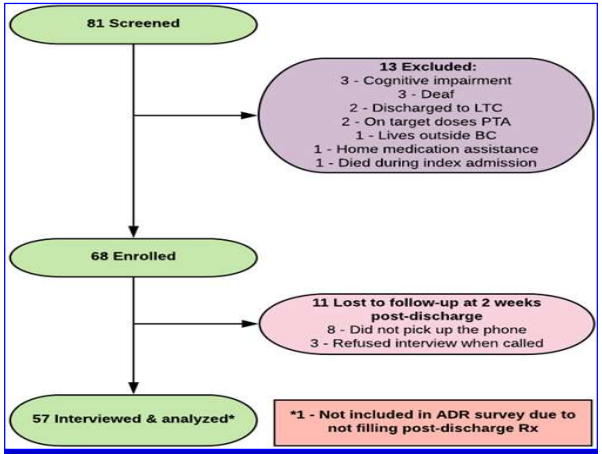

Figure 1. Study Flow Diagram

Table 1. Baseline Characteristics

Age (years)*	66 (51-80)
Male, n (%)	44 (65)
Length of stay ± SD (days)	4.5 ± 2.4
ACS type, n (%)	
STEMI	25 (37)
NSTEMI	39 (57)
UA	4 (6)
Treatment, n (%)	
Medical Management	15 (22)
PCI	53 (78)
Comorbidities, n (%)	
Hypertension	38 (56)
CAD	25 (37)
Diabetes	13 (19)
CVA	7 (10)
COPD	4 (6)
HF	3 (4)
CKD	3 (4)
PAD	2 (3)
Drug class prior to admission, n (%)	
Beta-Blocker	25 (37)
ACEI/ARB	28 (41)

*Reported as median (IQR)

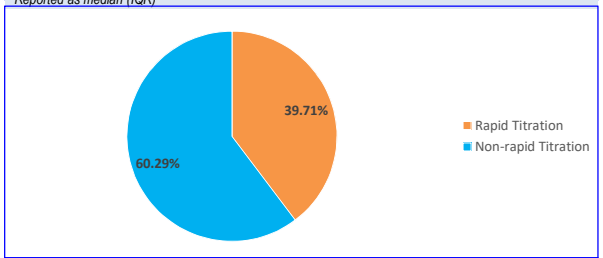

Figure 2. Distribution of Rapid and Non-rapid Titration Groups

Results

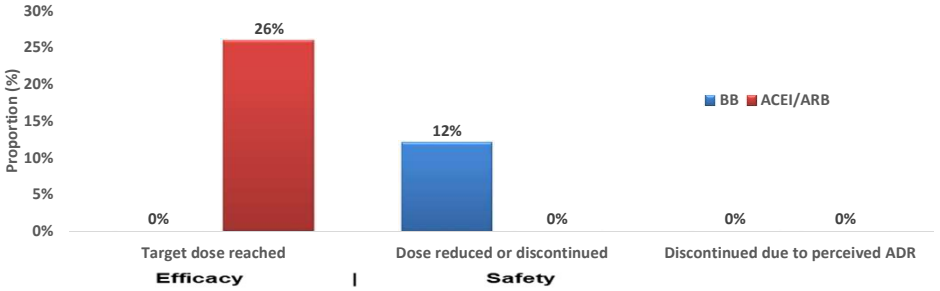

Figure 3. Efficacy and Safety Outcomes for Rapid Titration Group

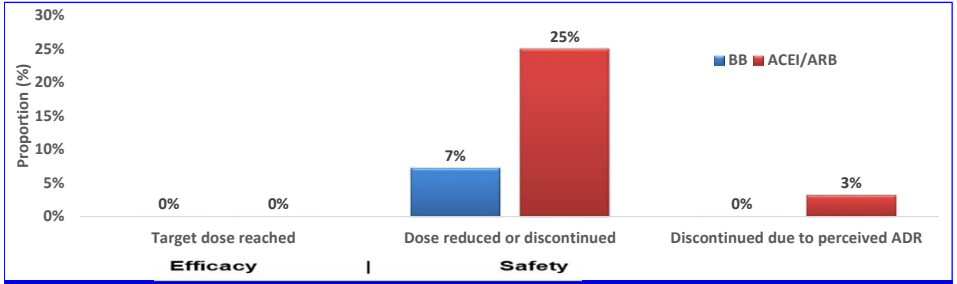

Figure 4. Efficacy and Safety Outcomes for Non-rapid Titration Group

Table 2. Incidence of Adverse Drug Reactions

	Rapid Titration, N (%)	Non-rapid Titration, N (%)
Experienced ≥ 1 ADRs	21 (84.0)	28 (87.5)
Fatigue	15 (60.0)	21 (65.6)
Fainting	4 (16.0)	9 (28.1)
Dizziness	3 (12.0)	11 (34.4)
Headaches	9 (36.0)	11 (34.4)
Insomnia	10 (40.0)	10 (31.3)
Dyspnea	15 (60.0)	19 (59.4)
Dry cough	3 (12.0)	7 (21.9)

*ADRs reported 2 weeks post-discharge

Discussion

- Higher rates of target doses in rapid titration group may be due to better physiologic reserve than non-rapid titration group
- Higher rates of dose reduction/discontinuation in the non-rapid titration group may be due to having a higher number of baseline comorbidities than the rapid titration group

Limitations

- Cross-sectional study design using small, non-randomized sample
- Confounders (i.e concomitant use of drugs with antihypertensive effects such as α_{1D} blockers) were not documented
- Social desirability bias, recall bias, and participant knowledge of post-discharge questionnaire may falsely lower dose reduction/discontinuation rates and reduce the true incidence of ADRs experienced
- Non-validated self-reported ADR assessment tool used for capturing ADRs

Conclusions

- Rapid titration of BB and ACEI/ARB post-ACS is less common than non-rapid titration
- Target dose achievement was uncommon in both rapid and non-rapid titration groups
- Dose reductions or discontinuations were uncommon in both rapid and non-rapid titration groups
- Dose reductions or discontinuations due to ADR were exceedingly rare
- An interventional study comparing rapid with non-rapid titration is necessary to fully evaluate efficacy and safety

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