Cost Consequences Analysis of Using Clevidipine in Cardiac Surgery from the perspective of a US hospital.

EE734

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INTRODUCTION

Background

- Rapid reduction of blood pressure (BP) with intravenous (IV) anti-hypertensive agents is required in various clinical settings when oral therapy is not feasible or not desirable.
- Clevidipine is an IV dihydropyridine calcium channel blocker indicated for the reduction of blood pressure.
- Clevidipine works by dilating arteries, thus reducing blood pressure. Clevidipine has a fast onset and offset of action making it easily adjustable to achieve desired blood pressure levels.

Objective

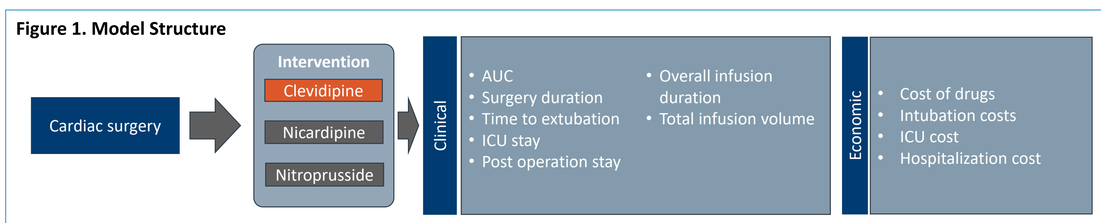
- The aim of this cost consequence analysis was to estimate the economics and consequences of varying clevidipine utilization for blood pressure management in patients undergoing cardiac surgery.

METHODS

Model Summary

- A decision analytic model was developed to simulate the costs and consequences associated with the use of clevidipine, sodium nitroprusside, and nicardipine in patients undergoing cardiac surgery experiencing perioperative hypertension.(**Figure 1**)
- Outcomes were quantified from a US hospital perspective over a 3-year time horizon.

Figure 1. Model Structure



Area Under the Curve (AUC); Intensive Care Unit (ICU)

Model Inputs

- The model inputs included utilization, dosing information, total mean initial hospital costs by level of control, health resource utilization (HRU) costs, and drug costs
  - Level of blood pressure control is measured by area under the curve (AUC).
    - Patients who are considered controlled have an AUC≤10 mm Hg x min/h and patients who are considered uncontrolled have an AUC>10 mm Hg x min/h.

Utilization

- The utilization of IV anti-hypertensives was calculated based on a retrospective analysis of CV-drug purchase history and Definitive Healthcare claims from 2021.[1] **(Table 1).**
- Diagnosis Related Group (DRG) codes were used to define CV-claims.
  - Medicare Severity Diagnosis Related Groups (MS-DRGs) included: 216, 217, 218, 219,220, 221, 231, 232, 233, 234,235, 236, 266, 267,319, and 320.
  - Hospitals above 204 cardiovascular claims (median) were included in the IV anti-hypertensive utilization analysis.
  - Low (cohort 1) and high(cohort 2) clevidipine adopter profiles were formed calculating the average utilization for clevidipine, sodium nitroprusside and nicardipine.
    - Cohort 1 represents the low adopter profile with <10% clevidipine utilization.
    - Cohort 2 represents the high adopter profile with ≥10% clevidipine utilization.
- The utilization of nicardipine Ready-to-Use (RTU) (0.1 mg/mL) and nicardipine vials are assumed to be equal.

Table 1. Projected IV Anti-hypertensive drug market share

Agent	Base Year (Cohort 1)	Year 1	Year 2	Year 3 (Cohort 2)
Clevidipine	1.3%	16.0%	30.8%	45.6%
Sodium Nitroprusside	4.4%	4.0%	3.5%	3.0%
Nicardipine	94.3%	80.0%	65.7%	51.4%
Total	100%	100%	100%	100%

Note: Percentages are rounded to one decimal and may not add to 100% as shown

Clinical Inputs

- The clinical inputs for AUC, surgery duration, intubation time, were based on published literature.[2-5] **(Table 2)**
- The cardiac analysis is based on 3 parallel studies (ECLIPSE) which included CABG, heart valve and combined CABG and heart valve procedures. SBP target ranges were 75-145 mmHg (pre- and post-operative) and 65-135 mmHg (intra-operative).
- Only pairwise comparisons of IV anti-hypertensives treatments have been reported vs clevidipine. Assumptions for clevidipine are based on pooled outcomes.
- A naïve indirect treatment comparison (e.g., not adjusting for differences in patient characteristics) was implemented using relative changes in outcomes observed from the individual pairwise comparisons from the ECLIPSE study, to approximate the indirect treatment effects relative to the pooled clevidipine outcomes.
- Outcomes that were adjusted in this way are: AUC ≤ 10 mm Hg*min/h, AUC > 10 mm Hg*min/h, surgery duration, intubation time, ICU time.
- Average infusion duration was informed by published literature.[6]

Table 2. Clinical inputs

	Clevidipine	Nicardipine	Nitroprusside
Controlled BP : AUC_{SBP-D} ≤ 10 mm Hg min/h[2]	56.60%	56.03%	41.22%
Surgery duration (h)[3]	3.3	3.4	3.5
Intubation (h)	7.0	7.9	7.7
≤ 6 h (% Pts)[4]	53.7%	53.7%	53.7%
6 h - 24 h (% Pts)[4]	37.9%	37.9%	37.9%
> 24 h (% Pts)[4]	8.4%	8.4%	8.4%
Total LOS (ICU, OR, GW) (h)[3]	32	33.4	34.3
Post-op LOS (days)	5.25	5.25	5.25
% Pts using 1 IV anti-HTN[5]	96.7%	51%	22%
% Pts using 2 IV anti-HTN[5]	3.3%	28%	32%
% Patient using 3 or more IV anti-HTN[5]	0.0%	21%	46%
Total (% Pts using 1-3 IV anti-HTN)	100%	100%	100%
Calculated weighted average # of IV anti-HTN	1.90	1.70	2.24

Table 3. Dosing information

	Clevidipine	Nicardipine	Nitroprusside
Average infusion duration (h)[6]	6.7	7.9	5.4
Average infusion rate (mg/h)[6-8]	5.2	8.0	4.3
Concentration (mg/mL)[7,8]	0.5	0.10	0.50

- The average infusion rate was calculated using customer survey data[9] and the prescribing information.[6-8] Dosing details were informed by the prescribing information.[7,8] **(Table 3)**

Economic Inputs

- The cost data is based on the ECLIPSE analysis for the weighted average for CABG, heart valve and combined CABG and heart valve procedures.[2]
- The total mean hospital costs by AUC for cardiac surgery and the HRU costs were based on published literature. (Table 4)
- For the hospital costs the model uses the estimate for all surgeries as the total hospital costs and it was defined as the sum of the cost of the initial hospitalization and any hospital costs incurred post-discharge due to complications within the 30 days following initial drug administration.[2]
- In the HRU costs, all cardiac surgery patients had a charge for mechanical ventilation on day 1, costs for mechanical ventilation on post-operative day 2 were used to calculated the incremental cost of mechanical ventilation
- Where needed, all costs have been adjusted to 2022 USD using Medical Care Consumer Price Index based on Federal Reserve Economic data.[10]

Table 4. Hospitalization and HRU Costs

Parameter	Mean
OR cost (hour)[3]	$1,899
ICU room and board (hour)[3]	$111
Post-ICU/regular wardroom and board (hour)[3]	$58
Ventilation cost on the second day of CABG (hour)[3]	$131
Hospital costs AUC ≤10[1]	$74,490
Hospital costs AUC >10[1]	$81,912

- The drug acquisition costs were informed by wholesale acquisition costs (WAC) from ProspectoRx.com.[11] **(Table 5)**

Table 5. Acquisition Costs

Agent	NDC code	Utilization	Acquisition price/ml[12]
Nicardipine vial	72572-0470-01	50%	$0.19
Nicardipine RTU	0143-9634-10	50%	$0.51
Clevidipine	10122-0610-01	NA	$1.46
Sodium nitroprusside	70436-0028-80		$0.02

RESULTS

- For a hypothetical caseload of 100 cardiac surgery patients, increased clevidipine use led to reductions in the length of stay (i.e., ICU, OR, and general ward) by 63 hours in total, which resulted in an average cost saving of $15,697.**(Table 6)**
- On a per patient basis, the increased use of clevidipine led to:
  - Slightly reduced surgery duration by 0.04 hours. **(Figure 2a)**
  - Slightly reduced intubation time by 0.4 hours. **(Figure 2b)**
  - ICU, OR, general ward length of stay by 0.6 hours. **(Figure 2c)**
  - Reduction in the IV anti-hypertensive average infusion volume by 242 mL. **(Figure 2d)**
  - Slightly lowered hospital costs resulting in an average cost saving of $35/patient including lower drug cost of about $34/patient. **(Figure 2e and Figure 2f)**

Table 6. Selected Total Hospital Cardiac Surgery Results (All patients)

	Base Case	1 year	2 year	3 year
Total LOS (hours)	3342	3321	3300	3279
Total hospital costs	$7,780,150	$7,779,017	$7,777,879	$7,776,737
Total IV anti-hypertensive drug costs	$22,312	$21,604	$20,491	$18,977
Total ICU, OR, GW LOS costs	$1,047,692	$1,042,466	$1,037,230	$1,031,995
Total ventilation costs on the second day of CABG	$103,224	$101,498	$99,768	$98,040

Figure 2 : Results per patient

Figure 2a. Surgery duration (Hours)

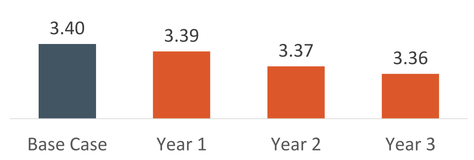


Figure 2b. Intubation duration (Hours)

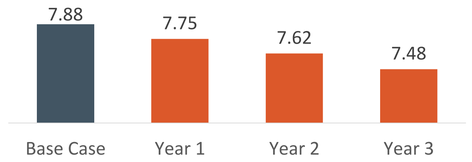


Figure 2c. ICU, OR, General ward length of stay (Hours)

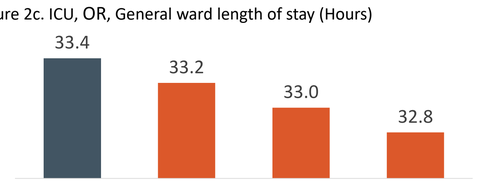


Figure 2d. Total IV anti-hypertensive infusion volume (mL)

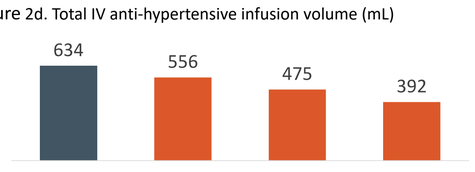


Figure 2e. Total hospital costs ($)

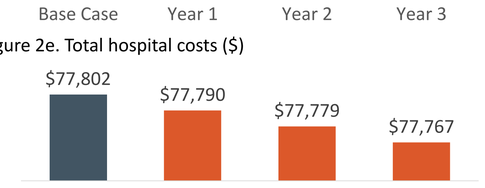
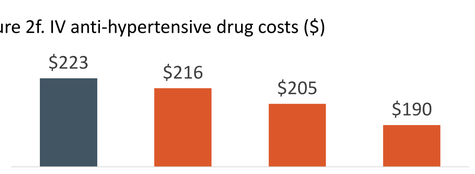


Figure 2f. IV anti-hypertensive drug costs ($)



CONCLUSION

- The increased use of clevidipine in cardiac surgery patients results in improved outcomes over the 3 years.
- The surgery duration, intubation duration and ICU, OR, General ward length of the stay were decreased slightly over the 3 years
- Cost savings were estimated over the 3 years, especially due to a reduction in total hospital stay.
- Additionally, IV anti-hypertensive drug costs were decreased with the reduction in the total infusion volume per patient

ASSUMPTIONS AND LIMITATIONS

- The safety and efficacy of clevidipine and the concomitant use of vasopressors has not been well-established and requires further prospective research.
- Vasopressors are excluded from the analysis. When not selected, utilization is not included for costing purposes; and outcomes such as volume are quantified. Vasopressors may be used in conjunction with IV anti-hypertensives which could impact costs and outcomes. The analysis is focused on IV anti-hypertensives.

DISCLOSURES
IJ, AS, are PRECISIONheor consultants for Chiesi USA, Inc. and received grants/research funding; and MG, SW, AC and EP are employees of Chiesi USA, Inc

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