

Association Between Hypotension and Drug Interaction of Direct-Acting Antiviral Agents in Hepatitis C Virus-Infected Patients: A Multicenter Study in Taiwan

CO162



Ting-Hsuan Hsu¹, Kai-Cheng Chang¹, Shih-Chieh Shao², Yuk-Ying Chan³, Hui-Yu Chen¹

¹Department of Pharmacy, Linkou Chang Gung Memorial Hospital, Taoyuan, Taiwan.

²Department of Pharmacy, Keelung Chang Gung Memorial Hospital, Keelung, Taiwan.

³Department of Pharmacy Administration, Chang Gung Medical Foundation, Taoyuan, Taiwan.

Background

- The effects of anti-hypertensive drugs could be potentiated by the drug-drug interaction (DDI) with direct-acting antiviral agents (DAAs) through the inhibition of P-glycoprotein and/or cytochrome P450, especially in hepatitis C virus (HCV) infected patients with polypharmacy.
- Real-world clinical significance of hypotension caused by DAA-related DDI has not been well-evaluated and needs to be characterized.

Objective

- To analyze the impact of DDIs on the change of blood pressure (BP).
- To explore the association between hypotension and drug interaction of DAA(s).

Methods

Study period 2017/5/1-2022/2/28

Study design Multi-centered, retrospective cohort study

Data source Electronic medical records database

Study population

Inclusion criteria:

- ≥ 18 years old
- HCV-infected patients
- ≥ 1 examination for genotyping
- Completing DAA course:
 - Sofosbuvir/Velpatasvir (SOF/VEL)
 - Glecaprevir/Pibrentasvir (GLE/PIB)

Exclusion criteria:

- Patients without HCV viral load data
- Patients with poor medication adherence

Definition of hypotension

- Systolic BP measured < 90 mmHg
- International Classification of Diseases code:
 - ICD-9: 458.0, 458.1, 458.9, 785.50, 785.51, 785.59
 - ICD-10: I95.0, I95.1, I95.2, I95.8, I95.9, R57.0, R57.1, R57.8, R57.9

Screening of DAA-related DDI

- Database:** University of Liverpool HEP Drug Interaction Checker
- Severity:**
 - Contraindication
 - Potential interaction
 - Potential weak interaction
 - Without interaction or unknown

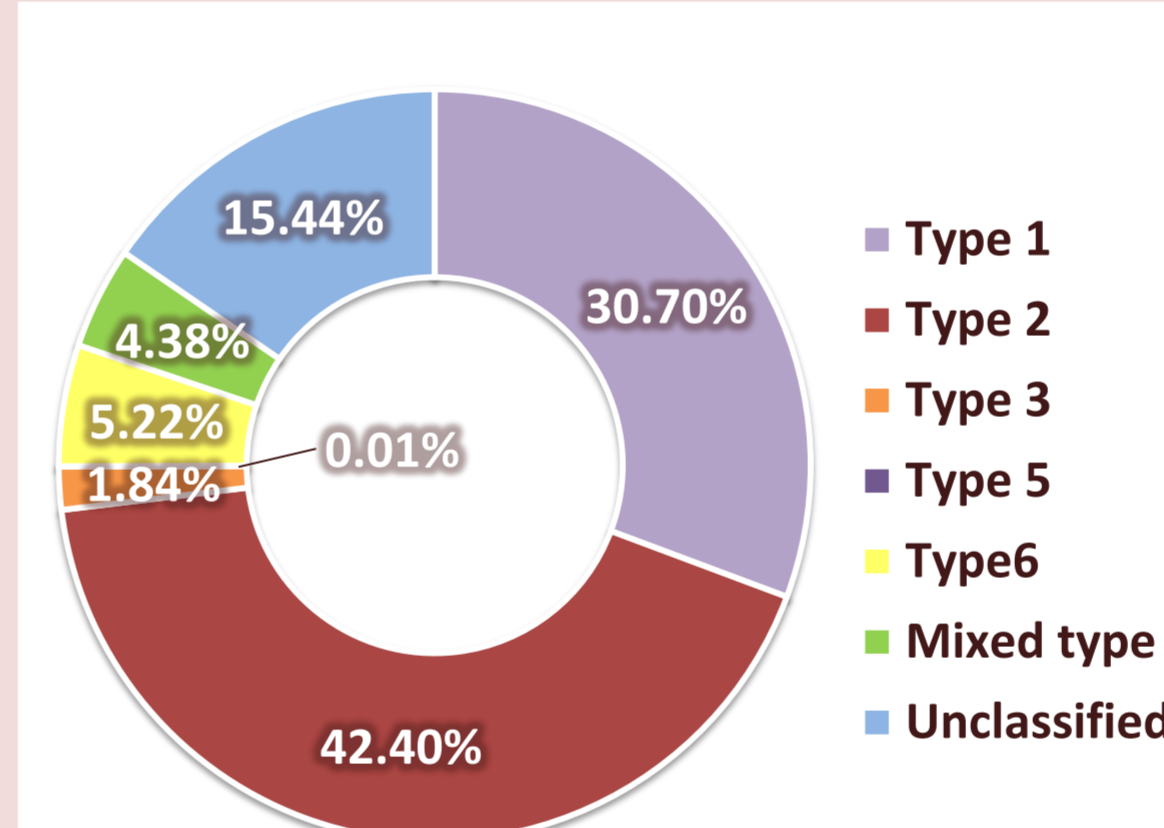
Logistic regression

- To estimate the association between the occurrence of DDI and hypotension.
- α=0.05 (two-sided)

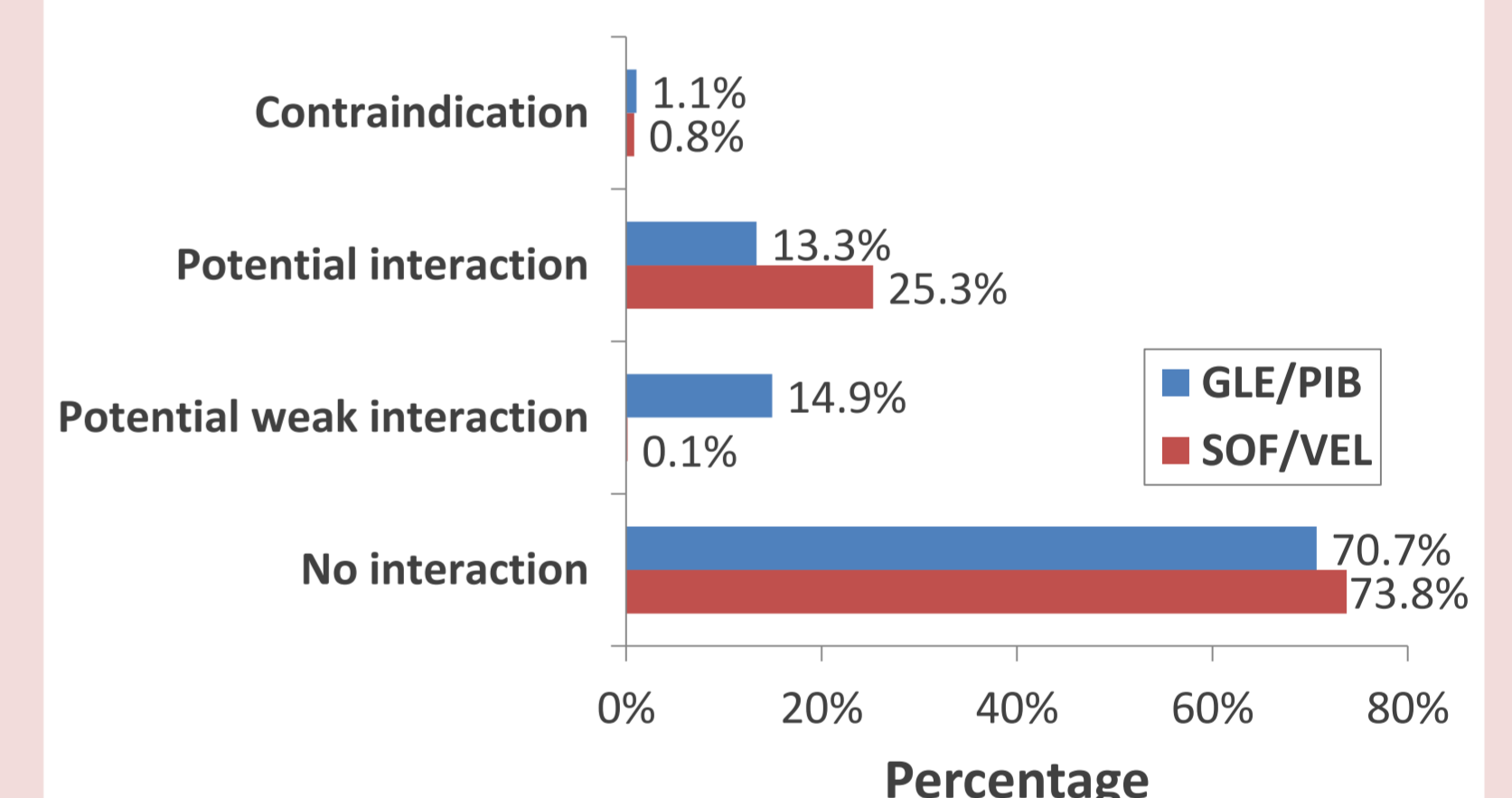
Baseline characteristics

Mean ± SD Median (IQR)	Total cohorts (N=6799)	SOF/VEL (n=3396)	GLE/PIB (n=3403)	p-value
Demographics				
Age (years)	62.0 ± 13.3	62.9 ± 13.6	61.1 ± 13.0	<.0001
Body Mass Index (kg/m ²)	24.9 ± 4.1	25.0 ± 4.3	24.7 ± 4.0	0.0875
Female, n (%)	3420 (50.3)	1667 (49.3)	1712 (50.7)	0.3139
HCV genotype, n (%)				
1	2087 (30.70)	1163 (55.7)	924 (44.3)	
2	2883 (42.39)	1271 (44.1)	1612 (55.9)	
3	125 (1.84)	54 (43.2)	71 (56.8)	
5	1 (0.01)	0 (0.0)	1 (100.0)	<.0001
6	355 (5.22)	167 (47.0)	188 (53.0)	
Mixed type	298 (4.38)	142 (47.7)	156 (52.3)	
Unclassified	1050 (15.44)	599 (57.0)	451 (43.0)	
Lab data				
eGFR (mL/min/1.73 m ²)	81.5 (63 – 97.5)	82.4 (65.6 – 98.7)	80.4 (59.8 – 96.6)	<.0001
FIB-4 score	2 (1.3 – 3.2)	2.1 (1.4 – 3.5)	1.9 (1.2 – 2.9)	<.0001
HCV RNA (mIU/mL)	3.6 ± 5.6	3.6 ± 6.1	3.6 ± 5.2	0.8494

HCV genotype



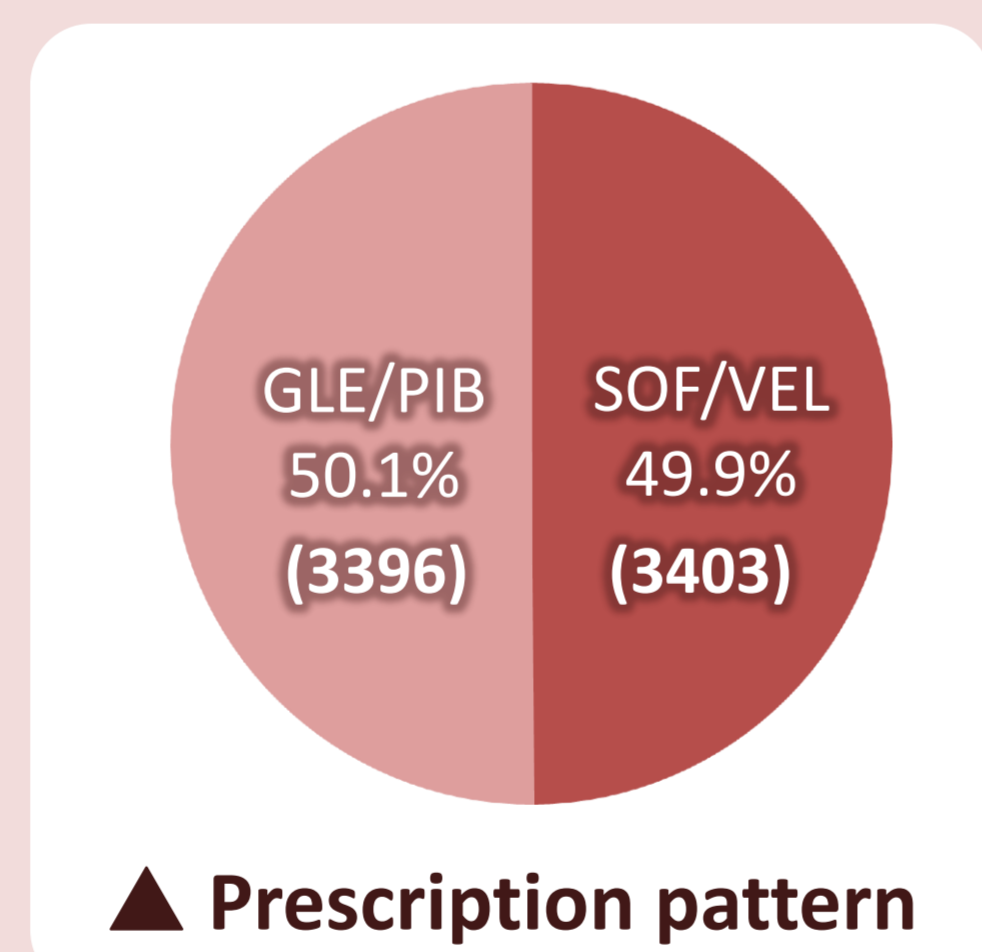
Real-world incidence of DDI



Results

Characteristics

- Sample size:** 6799 patients
- Gender:** ≈ 50% of female in both regimens
- Mean age:** 62.0 years old
- HCV genotype:** Type 2 HCV was in the majority



▲ Prescription pattern

Patients with DAA-related DDI...

- ↑ **Incidence rate of hypotension (in anti-hypertensive agent users)**
0.4% vs. 1.4%, p=0.0493
- ↑ **Odds of hypotension after controlling Charlson comorbidity index (CCI) (in GLE/PIB users with CCI= 1 – 2)**
Odds ratio= 4.5
95% CI= 1.5 – 13.4
- ↓ **Systolic blood pressure**
-8.7 vs. -11.3 mmHg, p < 0.0001

Incidence rates of hypotension

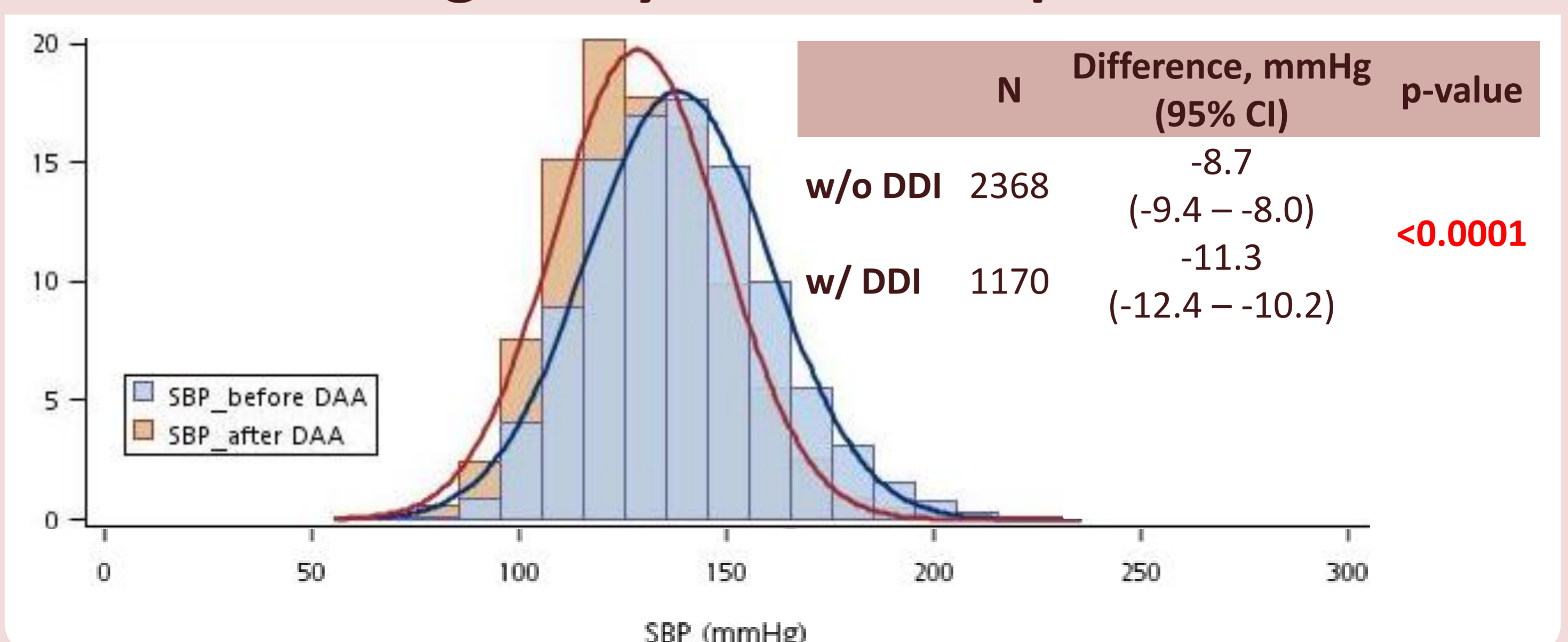
No. of anti-hypertensive agent users	No. of ADRs	w/o DDI	w/ DDI	p-value
1633	29	6 (0.4%)	23 (1.4%)	0.0493

Logistic regression analysis

DAA regimen	No. of DDIs	Charlson comorbidity index		
		1 – 2	3 – 4	≥ 5
SOF/VEL	w/o DDI (ref.)			
	≥ 1	2.6 (0.8 – 8.8)	0.5 (0.1 – 2.1)	1.8 (0.5 – 6.2)
GLE/PIB	w/o DDI (ref.)			
	≥ 1	4.5 (1.5 – 13.4)*	0.5 (0.1 – 2.9)	5.7 (0.7 – 46.2)

*p-value < 0.05

Change in systolic blood pressure



Conclusions

- Patients with DDI caused by DAA and anti-hypertensive agents were at risk of hypotension.
- Health care providers should be vigilant in identifying DAA-related DDIs and BP monitoring.
- Considering medication adjustment if needed.