

虚血性心疾患における β 遮断薬の適応：リアルワールドデータベースを用いた急性期循環動態に基づく有効性予測システムの開発

緒言：冠動脈疾患の予後改善に β 遮断薬が有用であることは広く知られている。しかしながら、実臨床では β 遮断薬の投与量は個々の臨床医の裁量で決定されており、投与量の参考になる指標はないのが実情である。

目的：リアルワールドデータベースを用いて冠動脈疾患患者における心拍数、 β 遮断薬と予後との関連を調べる。

方法：7 大学の心臓カテーテルデータベースから電子カルテデータを匿名化し、Standardized Structured Medical Information eXchange (SS-MIX2) を介して統合した 10,103 人の冠動脈疾患患者のデータのうち、退院時心拍数、 β 遮断薬、予後のデータのある 6,878 人を解析した。

結果：退院時心拍数を 4 群に分けたところ、 $HR \geq 75$ bpm の群はそれ以外の群と比較して有意に心血管イベントが多かった。急性冠症候群と安定冠動脈疾患に分けると、特に急性冠症候群において $HR \geq 75$ bpm 群が有意に予後不良であった。 β 遮断薬に関する解析において、カルベジロール群とビソプロロール群を比較したところ、ビソプロロール服用群の方がより退院時心拍数は低下していた。安定冠動脈疾患において、カルベジロール群と比較してビソプロロール群で予後改善効果がみられた。

結論：心拍数 75bpm 未満は冠動脈疾患患者における予後改善と関連していた。ビソプロロールはカルベジロールと比較して退院時心拍数の減少と関連していた。

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The relationships among the heart rate, use of β-blockers, and prognosis in patients with coronary artery disease in a real-world database using a storage system

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Background:

Increased HR has been associated with cardiovascular events not only in the general population or in individuals with cardiovascular risk factors¹⁻⁸) but also in patients with coronary artery disease (CAD)⁹). The use of β-blockers has the effect of improving the prognosis of patients with CAD¹⁰⁻¹⁴). One of the underlying mechanisms is a decrease in the cardiac load due to a reduction in the heart rate (HR)¹⁵⁻¹⁷). However, a lately report showed that there were no significant differences between bisoprolol and carvedilol despite the reduction in HR by bisoprolol, although a another

study showed that bisoprolol was more effective than carvedilol in decreasing the incidence of postdischarge atrial fibrillation in patients with CAD¹⁸).

Purpose:

To clarify the relationships among the HR, the use of β-blockers, and the prognosis in patients with CAD in a multicenter study using a storage system.

Methods:

The Clinical Deep Data Accumulation System (CLIDAS) collects (1) basic patient information, prescriptions, and laboratory data from electronic medical records from the Standardized Structured Medical Information eXchange (SS-MIX2) standard storage, and (2) the results of physiological tests, cardiac catheterization, and cardiac catheter intervention reports from the SS-MIX2 extended storage¹⁹⁻²¹). 10,103 cases who underwent cardiac catheterization from 6 university hospitals and the national cardiovascular center in Japan were registered (Figure 1).

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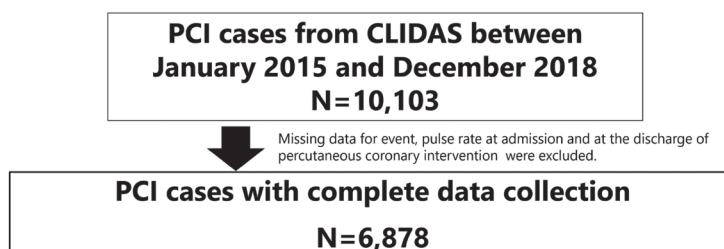


Figure 1 Study flow chart. CLIDAS: The Clinical Deep Data Accumulation System.

Results:

When we divided patients into quartile according to the HR at the discharge, the baseline characteristics has shown in table1. The highest quartile of HR group was associated with worse outcome than the other group (Figure 2). In addition, when we divided patients into the chronic coronary syndrome (CCS) group and the acute coronary syndrome (ACS) group, the highest quartile of HR group was associated with worse outcome especially in patients with ACS (Figure 3). We compared the pulse rate of the patients taking carvedilol and those taking bisoprolol at discharge. Bisoprolol was associated with a low HR than the carvedilol, although the effect of blood pressure reduction of bisoprolol is as same as that of carvedilol (Table 2). The use of

bisoprolol has more effect of improving the prognosis than that of carvedilol especially in patients with CCS (Figure 4).

Conclusion:

In a real-world database using a storage system, a HR of less than 75 bpm was associated with a good prognosis in patients with CAD. Bisoprolol was associated with a decreased HR at discharge compared to carvedilol.

Acknowledgments

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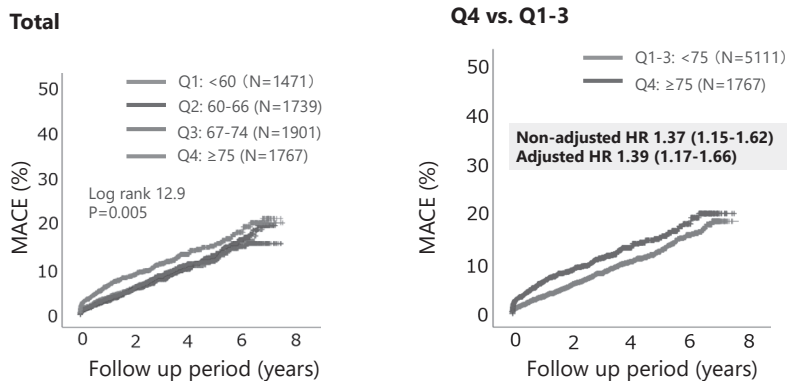


Figure 2 Kaplan-Meier curve for MACCE among patients into quartiles according to HR at discharge. Kaplan-Meier curve for MACCE between patients in combined Q1-Q3 groups and Q4. MACCE: major adverse cardiac and cerebral events.

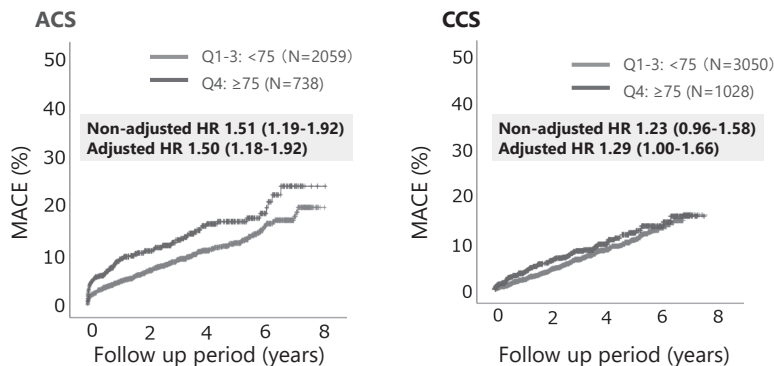


Figure 3 Kaplan-Meier curve for MACCE between patients in combined Q1-Q3 groups and Q4 in ACS. Kaplan-Meier curve for MACCE between patients in combined Q1-Q3 groups and Q4 in CCS. MACCE: major adverse cardiac and cerebral events; ACS: acute coronary syndrome; CCS: chronic coronary syndrome.

10 虚血性心疾患におけるβ遮断薬の適応：リアルワールドデータベースを用いた急性期循環動態に基づく有効性予測システムの開発

Table 1

	Q1-3 (N=5,111)	Q4 (N=1,767)	P
Age, years	70.5±10.7	69.0±11.9	<0.001
Male, %	78.3	76.4	0.091
Hypertension, %	82.8	80.1	0.010
Diabetes mellitus, %	42.7	47.4	0.001
Dyslipidemia, %	79.9	75.2	<0.001
Smoking, %	21.0	20.0	0.372
Systolic BP at the discharge, mmHg	120.0±23.1	118.9±31.3	0.138
Diastolic BP at the discharge, mmHg	65.2±11.4	67.4±12.3	<0.001
PR at the discharge, bpm	63.4±7.3	83.0±11.9	<0.001

Table 2

Patient characteristics	Carvedilol (N=1218)	Bisoprolol (N=2748)	P
Age, years	69.9±11.1	69.8±11.3	0.773
Male, %	78.1	76.5	0.285
Hypertension, %	82.6	83.3	0.525
Diabetes mellitus, %	49.8	41.7	<0.001
Dyslipidemia, %	78.4	80.4	0.147
Smoking, %	18.8	20.3	0.313
Systolic BP at the discharge, mmHg	118.8±19.6	118.0±27.8	0.308
Diastolic BP at the discharge, mmHg	66.0±12.1	65.5±11.9	0.274
PR at the discharge, bpm	68.4±12.5	66.9±12.5	0.001
PR ≥75 bpm, %	25.6	20.8	0.002

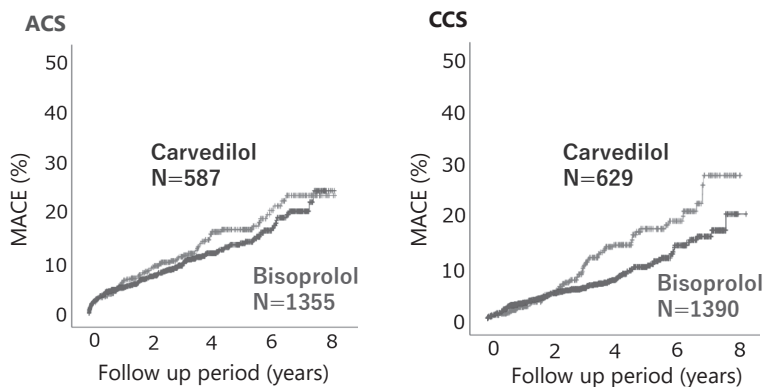


Figure 4 Kaplan–Meier curve for MACCE between the carvedilol and bisoprolol groups in ACS. Kaplan–Meier curve for MACCE between the carvedilol and bisoprolol groups in CCS. MACCE: major adverse cardiac and cerebral events; ACS: acute coronary syndrome; CCS: chronic coronary syndrome.

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- 12 虚血性心疾患における β 遮断薬の適応：リアルワールドデータベースを用いた急性期循環動態に基づく有効性予測システムの開発
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